European Medicines Agency
Evaluation of Medicines for Human Use

London, 17 November 2005
Doc. Ref. EMEA/CHMP/EWP/369929/2005

COMMITTEE FOR MEDICAL PRODUCT FOR HUMAN USE (CHMP)

RECOMMENDATION ON THE NEED FOR REVISION OF THE GUIDELINE ON CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS IN THE TREATMENT OF ALZHEIMER'S DISEASE (CPMP/EWP/553/95)

AGREED BY THE EFFICACY WORKING PARTY	27 September 2005
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	17 November 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	28 February 2006

The proposed guideline will replace the Guideline on Medicinal Products in the Treatment of Alzheimer's Disease (CPMP/EWP/553/95)

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1. INTRODUCTION

The term dementia describes a syndrome characterised by multiple impairments in cognitive functions without impairment in conscience. The cognitive functions that can be affected in dementia include general intelligence, learning and memory, language, problem solving, orientation, perception, attention and concentration, judgement and social abilities. These symptoms result in social and occupational decline.

2. PROBLEM STATEMENT

The dementia syndrome can have multiple aetiologies and pathophysiologies (e.g. Vascular Dementia, Mixed Dementia). Different drugs are developed directed towards either symptomatic improvement or to modification of aetiological and pathophysiological processes. In this respect treatment for prevention and arrest of disease progression in Alzheimer's disease are being evaluated. In addition studies have been performed in Minimal Cognitive Impairment.

The current guideline however, mainly deals with Alzheimer's disease.

Vascular dementia is generally regarded as the second most common form of dementia. Common features of vascular dementia include memory impairment, executive dysfunction, slow information processing, uninhibited behaviours and mood changes. Vascular dementia may present with an acute onset (due to multiple strokes or following a single "strategic stroke") or a more subacute onset (mainly caused by multiple ischemic-hypoxic white matter lesions and lacunae resulting from small vessel disease).

As Alzheimer's Disease and Vascular Dementia are both common disorders in the elderly they may coexist (mixed dementia). Moreover, both diseases share common risk factors such as hypertension, diabetes mellitus and apolipoprotein E status, which may play a complex role in both disease processes.

In vascular dementia the loss of executive function such as attention, working memory, planning, sequencing, abstraction and speed of mental processing dominates whereas in Alzheimer's disease memory and language problems are more dominant.

In addition patients with Alzheimer's disease usually gradually deteriorate over time, although the rate of decline varies with the stage of the disease (usually slower in early and late disease).

Mild cognitive impairment refers to patients with objectively established cognitive impairment which is not pronounced in more than one domain of cognition and does not seriously affect activities of daily living.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The existing guideline may need revision with respect to the scope of the guidance i.e. extension to other types of dementia e.g. vascular dementia, dementia with Lewy bodies and mixed types of dementias. If so the title of the document has to be changed.

The discussion may include:

- Reliable diagnostic criteria for the different dementias.

- Whether selection criteria, endpoints, study duration and other features in study design can be similar for the different types of dementias or should be different.

- The need and feasibility to in/exclude minimal cognitive impairment as a new concept (diagnostic criteria, validity, clinical relevance of the criteria chosen, appropriate primary outcome measure).

- The design of the study in Alzheimer's disease especially the duration of placebo controlled studies and the use of active controls.

- The need for a section concerning prevention and arrest of disease progression in Alzheimer's disease.

4. RECOMMENDATION

It is recommended to revise the CHMP Note for Guidance on Alzheimer's Disease incorporation the whole spectrum of dementias and addressing some new developments as described above.

5. PROPOSED TIMETABLE

It is anticipated that a draft revised CHMP guideline will be available 6 months after adoption of the recommendation.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The preparation of this Guideline will only involve the EWP.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is aimed that the revision of the guideline will be helpful to achieve more consensus in evaluation of such products by regulatory authorities. Furthermore, it is expected that such guidance document would improve quality of submitted studies by pharmaceutical industries.

8. INTERESTED PARTIES

- European College of Neuropsychopharmacology
- European Federation of Neurological Societies

9. REFERENCES TO LITERATURE, GUIDELINES ETC

- Current guideline on clinical investigation of medicinal products in the treatment of Alzheimer's Disease (CPMP/EWP/553/95).

