



European Medicines Agency
Evaluation of Medicines for Human Use

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**COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
(CHMP)**

**RECOMMENDATION ON THE NEED FOR REVISION OF THE GUIDELINE
ON CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS IN THE TREATMENT OF
PARKINSONS DISEASE
(CPMP/EWP/563/95)**

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 current guideline on clinical investigation of medicinal products in the treatment of Parkinson's Disease (CHMP/EWP/563/95)

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1. INTRODUCTION

Parkinson's disease is a common neurological disease with a gradual increase in prevalence after 50 years of age and a more steep increase in prevalence after 60 years of age. The incidence is estimated 18 per 100,000 per year and the prevalence about 360 per 100,000 per year. Parkinson's disease is a slowly progressive disease and severe disability-death may be expected in 25% of the patient within 5 years, in 65% of the patient within 10 years and in 80% of the patient within 15 years of disease onset.

The current NfG came into operation in June 1999 hence the need for a revision warrantS discussion.

2. PROBLEM STATEMENT

Several scientific issues have been triggered since the current NfG came into operation.

2.1 *Neuroprotective treatment*

Although no agent up to now is clearly neuroprotective, the number of trials evaluating products aiming to delay disease progression is increasing. Appropriate clinical development plan (phase II /III) as well as design and outcome measures of pivotal studies may need to be re-considered/extended.

2.2 *Treatment of (late) motor complications*

The treatment of late motor complications more and more implies polytherapy with more than 2 active products. From a methodological point of view it becomes increasingly difficult to attribute an observed effect to a genuine effect of the new product tested or to changes in co-medication during the trial for whatever reason. How to deal with this problem may need to be addressed more extensively in the revision.

2.3 *End of stage Parkinson's Disease*

Some products/devices combination have been developed for treatment in end of stage Parkinson's disease e.g. apomorphine. Hence, treatment in end of stage Parkinson's disease may warrant some remarks with regard to the appropriate study design for this condition.

2.4 *Neurotransplantation / Growth factors*

The revision may incorporate some guidance with respect to appropriate and acceptable study design for neurotransplantation when it includes a medicinal product e.g. need to show transplant survival, need for long term follow up etc. the same may hold for growth factors injected in the brain.

2.5 *Other aspects*

In the current guidance efficacy should be shown separately for dose-dependent and dose-independent motor complications. Whether this strict distinction can be maintained needs discussion.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

Recent development warrants a revision of the guidance concerning the development of agents in the treatment of Parkinson's disease.

4. RECOMMENDATION

The Working Party recommends revising the guideline on clinical investigation of medicinal products in the treatment of Parkinson's disease.

It is recommended to address end of stage Parkinson's disease and neurotransplantation / growth factors as new topics.

Revision is recommended with respect to neuroprotective treatment, and polytherapy for the treatment of motor complications.

It is recommended to re-discuss the appropriateness of the distinction between dose-dependent and dose-independent motor complications as separate indications.

It is recommended to discuss whether the scope of the guideline needs to be extended with respect to frequent Parkinson's disease associated co-morbidities.

5. PROPOSED TIMETABLE

It is expected that a draft revision of the guideline be released for consultation in 3/4Q2006.

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 studies submitted 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 Parkinson's Disease (CHMP/EWP/563/95).