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

# CONCEPT PAPER ON THE NEED FOR REVISION OF THE NOTE FOR GUIDANCE ON ANTIARRHYTHMICS (CPMP/EWP/237/95)

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## 1. INTRODUCTION

After a number of trials with anti-arrhythmics had show detrimental effects of some anti-anti-arrhythmics in patient with structural heart diseases, the popularity of these agents have declined dramatically, in particular those drugs that have class I and class III anti-arrhythmic effects. At the same time regulatory requirements have increased as indicated in the *CHMP NfG on anti-arrhythmics (CPMP/EWP/237/95*) that came into operation in June 1996. Since then, only a very small number of new drugs intended for the treatment of ventricular arrhythmias have been going through the central procedure and the same applies for the number of scientific advices for this purpose. As pro-arrhythmic effects appear to be less dominant in supraventricular arrhythmias, attention has focused on the prophylaxis and treatment of supraventricular arrhythmias, in particular atrial fibrillation/flutter. Issues have emerged that may warrant additional attention in the text of the aforementioned NfG.

## 2. PROBLEM STATEMENT

1. Patients with chronic atrial fibrillation/flutter are increasingly managed by slowing of the heart rate instead of cardioversion: rate control versus rhythm control. It has been shown that outcome in terms of morbidity and mortality is not significantly altered[1]. Criteria for rate control have been set and therefore slowing of the heart rate per se may be a method to assess efficacy in patients with chronic atrial fibrillation/flutter when the target is rate control. The issue whether reduction of morbidity and symptoms still need to be assessed separately needs to be discussed, provided that the respective data do not support a reasoned suspicion of a negative trend on life expectancy.

2. In some situations cardioversion may still be the primary aim of treatment in patients with supraventricular arrhythmias. This may be assessed by number of converters but time of conversions and recurrence rates need to be determined as well. This is currently not addressed in the *CHMP NfG on anti-arrhythmics (CPMP/EWP/237/95*.

## 3. MAIN TOPICS TO BE ADDRESSED

Guidance of the following issues should be given:

- Rate control in atrial fibrillation/flutter: reassessment of methods to assess efficacy and safety
- Rhythm control by chemical/electrical cardioversion in atrial fibrillation/flutter: methods to assess efficacy, goals of treatment, duration of conversion and recurrence rates

## 4. RECOMMENDATION

It is proposed to revise the *CPMP NfG on anti-arrhythmics (CPMP/EWP/237/95*) by specifically addressing a number of issues on the treatment of atrial fibrillation/flutter.

## 5. PROPOSED TIMETABLE

It is proposed that a first draft document is available for discussion at the EWP at March 2007.

## 6. RELEVANT REFERENCE

1. De Denus et al. Arch Intern Med 2005; 165: 258-62.