The European Agency for the Evaluation of Medicinal Products
Post-Authorisation Evaluation of Medicines for Human Use

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CPMP Position Statement

THE USE OF FIBRINOLYTICS IN DIABETIC PATIENTS

Introduction and background

Intravenous (iv) fibrinolytic agents[1] are indicated for the treatment of Acute Myocardial Infarction (AMI). Patients with diabetes *mellitus* are at an increased risk of AMI and subsequent morbidity and mortality, and thus clearly stand to benefit from fibrinolytic treatment. All iv fibrinolytic treatments currently licenced in the EU nonetheless include a contraindication or warning regarding use in patients with diabetic haemorrhagic retinopathy. Considering that in order to provide maximal benefit fibrinolytic therapy should be administered as soon as possible after diagnosis of AMI, a full medical history and detailed medical examination including fundoscopy is often impossible.

Discussion and conclusions

The medical rationale for the contraindication in these patients was based on a theoretically increased risk of retinal bleeding due to proliferative diabetic retinopathy, rather than evidence from clinical trial or post-marketing findings. In this respect, the CPMP has recently undertaken a comprehensive review of published data and pharmacovigilance databases and found that the number of spontaneous and clinical trial reports of retinal haemorrhage following iv administration of fibrinolytic agents for the treatment of AMI is extremely small. On the other hand there is clear evidence of reduced cardiac morbidity and mortality and of a reduction in total mortality following the use of fibrinolytics in patients with AMI.

On the basis of all the data available to the Committee, the CPMP concluded that the risk of intraocular haemorrhage is therefore outweighed by the increased chance of survival and reduced cardiac morbidity for the diabetic patient treated early with fibrinolytic therapy. The CPMP also noted that the European Society of Cardiology guidelines, published in September 2002, as well as the American Cardiological Guidelines stress that diabetes, and more particularly diabetic retinopathy, is not a contraindication to fibrinolytic therapy.

Therefore, it is important to provide clear, unambiguous guidance to medical and paramedical staff with respect to the use of iv fibrinolytic therapy in this clinical setting.

Recommendation

In the context of treatment of AMI the CPMP recommends the removal of the contraindications and warnings for use of iv fibrinolytics in diabetic patients or those with diabetic retinopathy.

For centrally authorised products, the EMEA has contacted the relevant Marketing Authorisation Holders to implement this recommendation through a type II variation procedure. For Nationally authorised products, this recommendation has been brought to the attention of the national competent authorities for further action as appropriate.

[1] Currently approved iv fibrinolytics in the EU include tenecteplase, reteplase, alteplase, anistreplase, streptokinase and urokinase.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74188400 Fax (44-20) 74188668
E-mail: mail@emea.eu.int http://www.emea.eu.int