PART VI SUMMARY OF THE RISK MANAGEMENT PLAN

SUMMARY OF RISK MANAGEMENT PLAN FOR ACTILYSE (ALTEPLASE)

This is a summary of the RMP for Actilyse (alteplase). The RMP details important risks of Actilyse, how these risks can be minimised, and how more information will be obtained about Actilyse's risks and uncertainties (missing information).

Actilyse's SmPC and its PL give essential information to healthcare professionals and patients on how Actilyse should be used.

I. THE MEDICINE AND WHAT IT IS USED FOR

Actilyse is authorised for the indications Thrombolytic treatment in acute myocardial infarction, Thrombolytic treatment in acute massive pulmonary embolism with haemodynamic instability, and Thrombolytic treatment of acute ischaemic stroke in the EEA (see SmPC for the full indication). It contains alteplase as the active substance and it is given by injection.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Actilyse, together with measures to minimise such risks and the proposed studies for learning more about Actilyse's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

If important information that may affect the safe use of Actilyse is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Actilyse are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered.
Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Actilyse. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information

PVI.Table 1 Summary of safety concerns

Important identified risks	None
Important potential risks	None
Missing information	Minor strokes Children Elderly Pregnancy and Lactation

II.B Summary of important risks

All important identified and potential risks were demoted.

The following table presents the remaining missing information.

Minor strokes	
Risk minimisation measures	SmPC sections 4.3 and 4.4, PL section 2. Actilyse is available as a prescription-only medicine. Actilyse is administered in a hospital setting only, by trained medical personnel. The use of Actilyse is restricted to physicians experienced in the treatment of stroke and neurovascular care
Children	
Risk minimisation measures	Actilyse is available as a prescription-only medicine. Actilyse is administered in a hospital setting only, by trained medical personnel. The use of Actilyse is restricted to physicians experienced in the treatment of stroke and neurovascular care.
Additional pharmacovigilance activities	Continuous monitoring and periodic (every 6 months) case by case review is performed in order to continuously evaluate efficacy and safety of alteplase use for the treatment of acute ischemic stroke in paediatric patients. within the SITS environment. The data extraction from the SITS environment is planed for 3 years or until data from 50 cases of 16-17 year old patients have been generated.
Elderly	
Risk minimisation measures	SmPC section 4.4 and PL section 2. Actilyse is available as a prescription-only medicine. Actilyse is administered in a hospital setting only, by trained medical personnel. The use of Actilyse is restricted to physicians experienced in the treatment of stroke and neurovascular care.

Additional pharmacovigilance activities	The registry aims to evaluate the proportions of SICH, death and functional independence/favourable outcome for ischaemic stroke patients treated with rt-PA in clinical routine settings. In the SITS-IVT >80 years post-approval registry it is planned to recruit approximately 1000 patients older than 80 years treated with intraveneous alteplase otherwise fulfilling SmPC criteria over a period of 3 years. At least 500 patients should be registered from centres in European countries that are part of the MRP. If the targeted 1000 patients is not reached during the 3 year period, the study will stop recruiting provided at least 500 patients from MRP countries are registered.
Pregnancy and Lactation	
Risk minimisation measures	SmPC section 4.6 and PL section 2. Actilyse is available as a prescription-only medicine. Actilyse is administered in a hospital setting only, by trained medical personnel. The use of Actilyse is restricted to physicians experienced in the treatment of stroke and neurovascular care.

II.C POST-AUTHORISATION DEVELOPMENT PLAN

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Actilyse.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Actilyse, however 2 data collecting programmes (SITS-IVT in elderly >80 years and consecutive single paediatric case assessment [for 3 years or until data from 50 cases of 16-17 year old patients have been generated], data derived from SITS environment) are ongoing.

ABBREVIATIONS

EEA	European Economic Area
MRP	Mutual recognition procedure
PL	Package leaflet
RMP	Risk management plan
rt-PA	Recombinant tissue-type plasminogen activator, alteplase
SICH	Symptomatic IntraCerebral Haemorrhage
SITS	Safe Implementation of Treatment in Stroke
SITS-IVT	Safe implementation of treatments in stroke – intravenuous thrombolysis in acute ischaemic stroke
SmPC	Summary of product characteristics