Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Metalyse 5 000 units (25 mg)
powder for solution for injection

tenecteplase

PLGB 14598/0240

Boehringer Ingelheim International GmbH

LAY SUMMARY

Metalyse 5 000 units (25 mg) powder for solution for injection
tenecteplase

This is a summary of the Public Assessment Report (PAR) for Metalyse 5 000 units (25 mg) powder for solution for injection. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Metalyse in this lay summary for ease of reading.

This application was approved under International Recognition procedure (IRP). The Reference Regulator (RR) was the European Medicines Agency (EMA), with the procedure number (EMEA/H/C/000306/II/0070/G). The procedure followed route A.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

For practical information about using Metalyse, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Metalyse and what is it used for?
This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

Metalyse is used in adults to treat stroke caused by a blood clot in an artery of the brain (acute ischaemic stroke) when it has been less than 4.5 hours since last seen without the symptoms of the current stroke.

How does Metalyse work?
Metalyse belongs to a group of medicines called thrombolytic agents. These medicines help to dissolve blood clots. Tenecteplase is a recombinant fibrin-specific plasminogen activator.

How is Metalyse used?
The pharmaceutical form of this medicine is a powder for solution of injection and the route of administration is intravenous (into a vein).

The patient's doctor will calculate the dose of Metalyse according to the patient's bodyweight, based on the following scheme:

Bodyweight (kg)	less than 60	60 to 70	70 to 80	80 to 90	Above 90
Metalyse (U)	3 000	3 500	4 000	4 500	5 000

Metalyse is given by a single injection into a vein by a doctor who is experienced in the use of this type of medicinal product.

The patient's doctor will give Metalyse as soon as possible after stroke starts as a single dose.

For further information on how Metalyse is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Metalyse have been shown in studies?
Studies in patients included tests to determine that this product is comparable to the already authorised strengths of this medicine.

The clinical studies that support the medical uses (indications) of this product are introduced below:

Acute ischaemic stroke
In a main study involving 1,577 adults who had an acute ischaemic stroke, Metalyse was at least as effective as alteplase at reducing the level of disability patients experienced after the stroke. Levels of disability were evaluated using the modified Rankin scale (mRS), a 7-point scoring system which measures the degree of disability or level of dependence in daily activities of people who had a stroke. Higher scores indicate more severe levels of disability or dependence. After 90 to 120 days following the stroke, around 37% of patients given Metalyse had an mRS score of 0 (no symptoms related to the nervous system) or 1 (no significant disability despite symptoms related to the nervous system) compared to around 35% of patients given alteplase.

What are the possible side effects of Metalyse?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effect with Metalyse (which can affect up to 1 in 10 people) includes haemorrhage (bleeding). The most common bleedings (which can affect up to 1 in 100 people) are epistaxis (nosebleeds), gastrointestinal haemorrhage (bleeding in the stomach or gut), ecchymosis (bleeding beneath the skin), urogenital haemorrhage (bleeding from the structures that carry urine or from the genital area), bleeding at the injection site, and at the skin puncture site.

Why was Metalyse approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Metalyse?
As for all newly-authorised medicines, an Risk Management Plan (RMP) has been developed for Metalyse. The RMP details the important risks of Metalyse, how these risks can be minimised, any uncertainties about Metalyse (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Metalyse.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Metalyse are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Metalyse
A marketing authorisation was granted in Great Britain on 26 April 2024.

The full PAR for Metalyse follows this summary.

This summary was last updated in June 2024.

TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Metalyse 5 000 units (25 mg) powder for solution for injection (PLGB 14598/0240) could be approved.

The product is approved for the following indications in adults:

- indicated in adults for the thrombolytic treatment of acute ischaemic stroke (AIS) within 4.5 hours from last known well and after exclusion of intracranial haemorrhage.

Tenecteplase is a recombinant fibrin-specific plasminogen activator that is derived from native t-PA by modifications at three sites of the protein structure. It binds to the fibrin component of the thrombus (blood clot) and selectively converts thrombus-bound plasminogen to plasmin, which degrades the fibrin matrix of the thrombus. Tenecteplase has a higher fibrin specificity and greater resistance to inactivation by its endogenous inhibitor (PAI-1) compared to native t-PA.

This application was approved under International Recognition procedure (IRP). The Reference Regulator (RR) was the European Medicines Agency (EMA), with the procedure number (EMEA/H/C/000306/II/0070/G). For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the reference regulator, please refer to the public assessment report on the relevant competent authority's website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended). This application is a line extension of the existing product range of Metalyse products (8 000 units and 10 000 units) to add a new strength of 5 000 units (25 mg) with a new indication (acute ischaemic stroke).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation was granted on 26 April 2024.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The quality of the product is acceptable, and no non-clinical or clinical safety concerns have been identified. Clinical experience with tenecteplase is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

I. TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**