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Advice document
SMC2697

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

Boehringer Ingelheim Limited

04 October 2024

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

tenecteplase (Metalyse®) is accepted for use within NHSScotland.

Indication under review: in adults for the thrombolytic treatment of acute ischaemic stroke within 4.5 hours from last known well and after exclusion of intracranial haemorrhage.

Tenecteplase offers an additional treatment choice in the therapeutic class of antithrombotic agents.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Tenecteplase is a recombinant fibrin-specific plasminogen activator that is derived from native tissue plasminogen activator (t-PA). It binds to the fibrin component of the thrombus and selectively converts thrombus-bound plasminogen to plasmin, which degrades the fibrin matrix of the thrombus. The treatment effect is time-dependent; therefore, earlier treatment increases the probability of a favourable outcome.[1, 2]

Tenecteplase must be prescribed by physicians experienced in neurovascular care and the use of thrombolytic treatment, with the facilities to monitor that use. The 25 mg presentation of tenecteplase is only intended for use in acute ischaemic stroke. Tenecteplase should be administered on the basis of body weight. See Summary of Product Characteristics for further information.[1]

1.2. Relevant comparator(s)

Alteplase (Actilyse®) is another antithrombotic agent that has previously been accepted for use by SMC for fibrinolytic treatment of acute ischaemic stroke (AIS). Treatment must be started as early as possible within 4.5 hours after onset of the stroke symptoms and after exclusion of intracranial haemorrhage by appropriate imaging techniques (e.g. cranial computerised tomography or other diagnostic imaging method sensitive for the presence of haemorrhage) (SMC 714/11). The submitting company considered that alteplase is the most relevant comparator for this submission.

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

AcT was a phase III, multicentre, open-label, parallel-group, registry-linked, randomised, controlled, non-inferiority study, which recruited 1,600 patients across Canada aged 18 years or older.[3, 4] Patients had a diagnosis of ischaemic stroke causing disabling neurological deficit, presenting within 4·5 hours of symptom onset, and eligible for thrombolysis. Patients were randomised to receive tenecteplase (n=806) or alteplase (n=771). The primary outcome was the proportion of patients with modified Rankin Scale (mRS) score of 0 to 1 at 90 to 120 days after treatment, assessed via blinded review in the intention-to-treat (ITT) population. The mRS score is a seven-point ordered categorical scale from 0 to 6 for functional neurological outcome, with 0 indicating no neurological symptoms and 6 indicating death. Non-inferiority was met if the lower 95% confidence interval (CI) of the difference in the proportion of patients who met the primary outcome between tenecteplase and alteplase groups was more than –5%. The primary outcome was met in 36.9% (296 / 802) of patients receiving tenecteplase and 34.8% (266 / 765) of those receiving alteplase. The findings demonstrated that tenecteplase was non-inferior to alteplase for the primary outcome (unadjusted risk difference: 2.1% [95% CI: -2.6, 6.9].

Health-related quality of life (HRQL) outcomes were measured at 90 days using the EuroQol visual analogue scale (EQ-VAS) (n = 1,262) and EQ-5D-5L (n = 1,289) scales. Overall, no differences were observed between treatment arms for the EQ-VAS or EQ-5D-5L domains. In addition, no meaningful differences were observed between tenecteplase and alteplase in key safety outcomes such as the rate of 24-hour symptomatic intracerebral haemorrhage (3.4% versus 3.2%) or 90-day mortality (15.3% versus 15.4%). Orolingual angio-oedema (1.1% versus 1.2%) and extracranial bleeding requiring blood transfusion (0.8% in both groups) were rare and had similar occurrences in both groups.

EXTEND-IA TNK Part 1 was a phase II, multicentre, randomised, open-label, blinded-endpoint, non-inferiority study, which recruited 202 patients from Australia and New Zealand.[5, 6] Patients had presented with AIS within 4.5 hours of onset with large vessel occlusion of the internal carotid, middle cerebral or basilar artery, and were eligible to undergo intravenous (IV) thrombolysis and endovascular thrombectomy. Patients were randomised to receive tenecteplase (n=101) or alteplase (n=101). The primary outcome was the proportion of patients with substantial reperfusion (restoration of blood flow to >50% of the affected arterial territory or absence of retrievable thrombus at initial angiogram). The primary endpoint was met in 22% (22 patients) of patients in the tenecteplase group versus 10% (10 patients) in the alteplase group (incidence difference, 12 percentage points; 95% CI, 2 to 21; incidence ratio, 2.2; 95% CI, 1.1 to 4.4; P = 0.002 for non-inferiority). Tenecteplase resulted in a better 90-day functional outcome than alteplase. Similar efficacy was reported for some key secondary outcomes. Symptomatic intracerebral haemorrhage occurred in 1% of the patients in each group.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment*

The company estimated that there would be 1,000 patients eligible for treatment with tenecteplase each year. It is estimated that approximately 750 patients would receive tenecteplase in year 1 and 900 patients each year in years 2 to 5.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

References

1. Boehringer Ingelheim Limited. Tenecteplase (Metalyse®). Summary of Product Characteristics. Electronic Medicines Compendium. www.medicines.org.uk/emc/
2. The European Medicines Agency. European Public Assessment Report. Tenecteplase (Metalyse®). EMA/37096/2024. 14 December 2023. Available from Metalyse, INN-Tenecteplase (europa.eu).
3. Menon BK, Buck BH, Singh N, Deschaintre Y, Almekhlafi MA, Coutts SB, et al. Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial. Lancet. 2022;400(10347):161–9.
4. ClinicalTrials.gov. Alteplase Compared to Tenecteplase in Patients With Acute Ischemic Stroke (AcT; NCT03889249). Available from: https://clinicaltrials.gov/study/NCT03889249?intr=NCT03889249&rank=1 (Accessed 3 September 2024).
5. Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ, Dowling RJ, et al. Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke. *N Engl J Med.* 2018;378(17):1573–82.
6. ClinicalTrials.gov. Tenecteplase Versus Alteplase Before Endovascular Therapy for Ischemic Stroke ((EXTEND-IA TNK; NCT02388061). Available from: https://clinicaltrials.gov/study/NCT02388061?intr=NCT02388061&rank=1 (Accessed 3 September 2024)

This assessment is based on data submitted by the applicant company up to and including **03 June 2024.**

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial-in-confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.