

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Alteplase for the treatment of acute ischaemic stroke (review of technology appraisal 122)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of alteplase within its licensed indication for the treatment of acute ischaemic stroke (review of existing guidance 122).

Background

The word *stroke* refers to the clinical syndrome that occurs when there is an interruption of the blood supply to a localised area of the brain. There are two main types of stroke – ischaemic and haemorrhagic. An ischaemic stroke arises when there is a blockage in a blood vessel serving the brain caused by a blood clot (thrombus). A haemorrhagic stroke occurs when a blood vessel in or around the brain ruptures causing blood to leak out. Ischaemic strokes account for over 80% of all strokes.

Each year, over 130,000 people in England and Wales have a stroke. Mortality statistics from 2008 indicate that approximately 36,000 people died from stroke (ischaemic and haemorrhagic) in England and Wales.

Standard treatment for stroke includes supportive and medical management in a specialist centre during the acute phase (including thrombolysis where appropriate to break up blood clots), measures to prevent the damage to the brain from getting worse, and appropriate rehabilitative and physiotherapy programmes during the post stroke period. NICE technology appraisal 122 and clinical guideline 68 ('Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack') recommends thrombolysis with alteplase within 3 hours of symptom onset for adults with acute ischaemic stroke. Alteplase should only be used by physicians experienced in the management of acute stroke.

The technology

Alteplase (Actilyse, Boehringer Ingelheim) is a tissue plasminogen activator manufactured by recombinant DNA technology. It activates the production of plasmin from its precursor plasminogen. Plasmin is an enzyme which degrades fibrin clots. The aim of treatment is to reduce the impact of ischaemia by restoring blood flow through the occluded (or blocked) artery. It is administered by intravenous infusion.

Alteplase currently has a UK marketing authorisation for the fibrinolytic treatment of acute ischaemic stroke in adults aged 18-80 years. Treatment must be started within 3 hours of onset of the stroke symptoms and after prior exclusion of intracranial haemorrhage by means of appropriate imaging techniques.

An extension to the marketing authorisation is currently being sought which would allow an increase in the time window for alteplase use from within 3 hours of the onset of stroke symptoms to within 4.5 hours. Alteplase has been studied in a placebo-controlled trial and an observational study, when used between 3 and 4.5 hours after the onset of stroke symptoms, in adults with acute ischaemic stroke.

Intervention(s)	Alteplase
Population(s)	Adults with acute ischaemic stroke within 4.5 hours of symptom onset
Comparators	Standard medical and supportive management that does not include alteplase
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • disability (Modified Rankin Scale) • functional recovery • neurological deficit • change in mental health, including anxiety & depression • mortality • length of hospital stay • adverse effects of treatment, including bleeding events • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>

<p>Other considerations</p>	<p>If the evidence allows the following subgroup will be considered:</p> <ul style="list-style-type: none"> Subgroups by time to treatment (0-3 hours and 3-4.5 hours) <p>Guidance will only be issued in accordance with the marketing authorisation.</p>
<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 122, June 2007, Alteplase for the treatment of acute ischaemic stroke. Under review.</p> <p>Technology Appraisal No. 210, December 2010, Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (review of technology appraisal guidance 90). Review date July 2013.</p> <p>Related Guidelines:</p> <p>Clinical Guideline No. 67, May 2008, Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. Review decision date TBC.</p> <p>Clinical Guideline No. 68, July 2008, Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). Review date March 2012.</p> <p>Related Public Health Guidance/Guidelines:</p> <p>Public Health Guidance No. 25, June 2010, Prevention of cardiovascular disease at the population level.</p> <p>Related Quality Standards: Stroke Quality Standard. June 2010</p>