Proposed Health Technology Appraisal

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

Draft scope

Draft 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 degrading the blood clot that caused the ischaemia. 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	The outcome measures to be considered include: • 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	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If the evidence allows the following subgroup will be

	considered: • Subgroups by time to treatment (0-3 hours and 3-4.5 hours) Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 122, June 2007, Alteplase for the treatment of acute ischaemic stroke. Under review. 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. Related Guidelines: 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. Clinical Guideline No. 68, July 2008, Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). Review decision date December 2011. Related Public Health Guidance/Guidelines: Public Health Guidance No. 25, June 2010, Prevention of cardiovascular disease at the population level. Related Quality Standards: Stroke Quality Standard. June 2010

Questions for consultation

Has the most appropriate comparator for alteplase for the treatment of acute ischaemic stroke been included in the scope?

- How should standard medical management be defined?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need

to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)