Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ticagrelor for preventing thrombotic events in people with acute ischaemic stroke or transient ischaemic attack

Draft scope (pre-referral)

Draft remit/appraisal objective
To appraise the clinical and cost effectiveness of ticagrelor within its marketing authorisation for the prevention of thrombotic events in people with acute ischaemic stroke or transient ischaemic attack.

Background
A stroke is the interruption of the blood supply to a localised area of the brain. There are two main types of stroke. The first type, ischaemic stroke, arises when there is a blockage in a blood vessel serving the brain, caused, for example by a blood clot (thrombus). The second main type is haemorrhagic stroke, and this occurs when a blood vessel in or around the brain ruptures causing blood to leak out. A blockage in the blood supply to the brain accounts for 80% to 85% of strokes, and haemorrhage for 15% to 20%. A transient ischaemic attack (TIA), often called a 'mini-stroke', happens when the blood supply to part of the brain is interrupted for a short time. TIA is associated with a high risk of stroke in the first month after the event and up to a year afterwards.

Risk factors for stroke and TIA include smoking, hypertension, high cholesterol levels, excess alcohol intake, atrial fibrillation, and diabetes. In 2014/15, there were over 7,000 hospital admissions for stroke and 20,000 hospital admissions for transient ischaemic attack in England.

Standard treatment for stroke includes supportive and medical management in a specialist centre during the acute phase, 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 264 and clinical guideline 68 (‘Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack’) recommends thrombolysis with alteplase within 4.5 hours of onset of stroke symptoms. Treatment with aspirin is recommended for acute ischaemic stroke without primary intracerebral haemorrhage within 24 hours of symptom onset and continued for two weeks or until discharge if sooner.

NICE clinical guideline 68 recommends that people who have had a suspected TIA should be assessed for their risk of subsequent stroke using a validated scoring system such as ABCD. The guideline recommends treatment with aspirin for people with suspected TIA.
NICE has also produced guidance on the secondary prevention of occlusive vascular events following an ischaemic stroke or TIA. NICE technology appraisal 210 recommends clopidogrel as an option for people who have had an ischaemic stroke. It recommends modified-release dipyridamole in combination with aspirin as an option for people who have had a transient ischaemic attack or if clopidogrel is contraindicated or not tolerated.

**The technology**

Ticagrelor (Brilique, AstraZeneca) is an adenosine triphosphate analogue that binds reversibly to the P2Y12 class of adenosine diphosphate receptors on platelets and inhibits platelet activation and aggregation. It is administered orally.

Ticagrelor does not currently have a marketing authorisation in the UK for preventing thrombotic events in people with acute ischaemic stroke or transient ischaemic attack. It has been studied in a clinical trial, compared with aspirin in adults with either acute ischaemic stroke or high-risk transient ischaemic attack within 24 hours after onset of symptoms.

Ticagrelor in combination with aspirin, has a marketing authorisation in the UK for “the prevention of atherothrombotic events in adult patients with acute coronary syndromes (unstable angina, non ST elevation myocardial infarction or ST elevation myocardial infarction); including patients managed medically, and those who are managed with percutaneous coronary intervention or coronary artery by-pass grafting”.

<table>
<thead>
<tr>
<th>Intervention(s)</th>
<th>Ticagrelor</th>
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<tbody>
<tr>
<td>Population(s)</td>
<td>Adults with acute ischaemic stroke or transient ischaemic attack</td>
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<tr>
<td>Comparators</td>
<td>• Aspirin</td>
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### Outcomes

The outcome measures to be considered include:

- disability
- neurological deficit
- non-fatal myocardial infarction (STEMI and NSTEMI)
- non-fatal stroke
- bleeding events
- mortality
- adverse effects of treatment
- 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

Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.

### Related NICE recommendations and NICE Pathways

Related Technology Appraisals:


Related Guidelines:

- ‘Stroke rehabilitation in adults’ (2013). NICE guideline 162. Review proposal date: to be confirmed
- ‘Stroke and transient ischaemic attack in over 16s: diagnosis and initial management’ (2008). NICE
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Questions for consultation

Has the relevant comparator for ticagrelor been included in the scope?

- Are other treatments such as clopidogrel, prasugrel or modified-release dipyridamole used for treating acute ischaemic stroke or transient ischaemic attack in clinical practice?

- Should alteplase be considered as a comparator for ticagrelor?

In clinical practice, for treating transient ischaemic attack would ticagrelor be used for all patients or only a subgroup of patients?

- If ticagrelor would be used for only a subgroup, what are the characteristics of this subgroup?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom ticagrelor is expected to be more clinically effective and cost effective?

Where do you consider ticagrelor will fit into the existing NICE Stroke pathway?: http://pathways.nice.org.uk/pathways/stroke
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NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which ticagrelor will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider ticagrelor 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 ticagrelor 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/article/pmg19/chapter/1-Introduction)

References


3 Lui J and Wang LN. Peroxisome proliferator-activated receptor gamma agonists for preventing recurrent stroke and other vascular events in patients

National Institute for Health and Care Excellence
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with stroke or transient ischaemic attack (Review) (2014). Cochrane Database of Systematic Reviews.