NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ticagrelor for preventing stroke after previous ischaemic stroke or high-risk 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 preventing stroke after previous acute ischaemic stroke or high-risk transient ischaemic attack.

Background

A stroke occurs when the blood supply to part of the brain is cut off. About 85% of stroke cases are ischaemic stroke, where the blood supply to the brain is stopped because of a blood clot. A transient ischaemic attack (TIA) is a stroke that recovers within 24 hours of onset of symptoms. The ABCD2 scoring system may be used to identify people at high risk of a stroke after a TIA. It is calculated based on age, blood pressure, clinical features and duration of symptoms.

More than 100,000 strokes occur in the UK each year, and there are over 1.2 million stroke survivors in the UK[1]. Someone who has had a stroke is at increased risk of experiencing another stroke; around 39% will experience another stroke within 10 years[2]. The risk of recurrent events is highest soon after the first stroke, so it is important to start secondary prevention as soon as possible. Between 46,000 and 65,000 people in the UK are estimated to have a transient ischaemic attack (TIA) each year[3]. The risk of an ischemic stroke after a TIA is estimated to be 9%–17% at 90 days[4].

Options for secondary prevention of stroke may include antiplatelets or anticoagulants. Lifestyle modifications such as exercise, stopping smoking and reducing alcohol intake are important in reducing cardiovascular risk. Reducing blood pressure with antihypertensive treatment and lipid levels with statins also reduces the risk of further vascular events for people who have had a stroke[5].

For people who have had an ischaemic stroke, NICE technology appraisal 210 recommends clopidogrel to prevent occlusive vascular events. It recommends modified-release dipyridamole with aspirin if clopidogrel is contraindicated or not tolerated. It also recommends modified-release dipyridamole alone if aspirin and clopidogrel are contraindicated or not tolerated. The Royal College of Physicians' National Clinical Guideline for Stroke[5] recommends that aspirin may be used alone if both clopidogrel and modified-release dipyridamole are contraindicated or not tolerated.

For people who have had a TIA, NICE technology appraisal 210 recommends modified-release dipyridamole with aspirin, or modified-release dipyridamole alone if aspirin is contraindicated or not tolerated. The Royal College of Physicians' National Clinical Guideline for Stroke[5] recommends the same treatment for people who have had a TIA as for people who have had a stroke, that is, clopidogrel as the standard antithrombotic treatment.

The technology

Ticagrelor (Brillique, AstraZeneca) is an adenosine triphosphate analogue that binds 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 stroke after previous ischaemic stroke or high-risk transient ischaemic attack. Ticagrelor has a marketing authorisation in the UK for preventing atherothrombotic events in adults with acute coronary syndromes or a history of myocardial infarction and a high risk of developing an atherothrombotic event. It has been studied with aspirin in clinical trials compared with placebo with aspirin or clopidogrel with aspirin in people aged 40 and over who have had an acute ischaemic stroke or TIA with moderate-to-high risk of stroke recurrence.

Intervention(s)	Ticagrelor with a background of aspirin
Population(s)	People who have had an acute ischaemic stroke or TIA with high risk of stroke recurrence.
Comparators	• Clopidogrel (does not have a marketing authorisation in the UK for preventing stroke after previous TIA) • Modified-release dipyridamole with aspirin • Modified-release dipyridamole • Aspirin
Outcomes	The outcome measures to be considered include: • stroke events • disability • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If the evidence allows the following subgroups will be considered. These include people who have had a stroke and people who have had a TIA. 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:** Ticagrelor for preventing atherothrombotic events after myocardial infarction (2016) NICE technology appraisal guidance 420. Review in progress. Ticagrelor for the treatment of acute coronary syndromes (2011) NICE technology appraisal guidance 236. On static list. Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (2010) NICE technology appraisal guidance 210. On static list. **Appraisals in development (including suspended appraisals):** Ticagrelor for preventing cardiovascular events in people with type 2 diabetes and coronary artery disease NICE technology appraisal guidance. Publication date to be confirmed. **Related Guidelines:** Stroke and transient ischaemic attack in over 16s: diagnosis and initial management (2019) NICE guideline NG128 Cardiovascular disease: risk assessment and reduction, including lipid modification (2019) NICE technology appraisal

	CG181 Stroke rehabilitation in adults (2013) NICE guideline CG162 **Related Public Health Guidance/Guidelines:** Cardiovascular disease prevention (2010) NICE guideline PH25 **Related Quality Standards:** Stroke in adults (2010 updated 2016) NICE quality standard 2 Cardiovascular risk assessment and lipid modification (2015) NICE quality standard 100 **Related NICE Pathways:** Stroke (2019) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2017) Specialised Vascular Services (Adults). Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for ticagrelor with aspirin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for preventing stroke after previous acute ischaemic stroke or high-risk TIA? Is clopidogrel used in NHS practice to prevent stroke after previous TIA?

Are the outcomes listed appropriate?

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

Where do you consider ticagrelor with aspirin will fit into the existing NICE pathway, Stroke?

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 with aspirin 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 with aspirin 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Stroke Association (2018) State of the nation: stroke statistics. Accessed January 2020

2 Mohan KM, Wolfe CD, Rudd AG et al. (2011) Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. Stroke, 42: 1489-94

3 NICE (2013) Transient ischaemic attack: clopidogrel Evidence summary ESUOM23.

4 Gupta HV, Farrell AM, and Mittal MK (2014) Transient ischemic attacks: predictability of future ischemic stroke or transient ischemic attack events. Therapeutics and clinical risk management 10: 27-35

5 Royal College of Physicians (2016) National Clinical Guideline for Stroke. Accessed January 2020