

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Proposed Health Technology Appraisal**

**Ticagrelor for preventing cardiovascular events in people with type 2 diabetes and coronary artery disease**

**Draft scope (pre-referral)**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of ticagrelor within its marketing authorisation for preventing cardiovascular events in people with type 2 diabetes and coronary artery disease.

**Background**

Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance (that is, the body's inability to effectively use insulin) and insufficient pancreatic insulin production, resulting in high blood glucose levels (hyperglycaemia). It is commonly associated with obesity, physical inactivity, raised blood pressure, disturbed blood lipid levels and a tendency to develop thrombosis, and therefore is recognised to lead to an increased cardiovascular risk. It is also associated with long-term microvascular and macrovascular complications, together with reduced quality of life and life expectancy.

In 2016, there were approximately 3.1 million adults in England with diabetes, of whom 90% had type 2 diabetes<sup>1</sup>. However, many people with type 2 diabetes are undiagnosed, and so the number of people with the condition may be higher than reported. The prevalence of type 2 diabetes is rising because of increased prevalence of obesity, decreased physical activity and increased life expectancy after diagnosis because of better cardiovascular risk protection. More than 50% of type 2 diabetes patients will exhibit signs of cardiovascular disease complications at diagnosis and are more likely to be at risk from heart attacks, strokes and high blood pressure. Coronary artery disease is recognized to be the cause of death for 80% of people with diabetes<sup>2</sup>.

NICE guideline 181 recommends identifying and assessing cardiovascular disease (CVD) risks in patients with type 2 diabetes and the use of lipid modification therapy (atorvastatin) for secondary prevention of CVD and as primary prevention of CVD to people with type 2 diabetes who have a 10% or greater 10-year risk of developing CVD. This is in addition to lifestyle interventions such as changes to diet, physical activity, smoking and alcohol consumption.

NICE guideline 28 ([Type 2 diabetes in adults: management](#)) recommends that people with type 2 diabetes without cardiovascular disease should not be offered antiplatelet therapy (aspirin or clopidogrel) for the primary prevention

of CVD. NICE clinical knowledge summary ([Antiplatelet treatment](#)) suggests antiplatelet therapy as secondary prevention of cardiovascular events should be offered to people with acute coronary syndrome, angina, atrial fibrillation or peripheral arterial disease.

### The technology

Ticagrelor (Brilique, 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 cardiovascular events in people with type 2 diabetes and coronary artery disease. It has been studied in a clinical trial, compared with placebo in adults with type 2 diabetes mellitus and coronary artery occlusive disease; who have been treated with a glucose lowering medication for at least 6 months.

Ticagrelor co-administered 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” and “for the prevention of atherothrombotic events in adults who have had a myocardial infarction and who are at high risk of a further event”.

<b>Intervention(s)</b>	Ticagrelor
<b>Population(s)</b>	People with type 2 diabetes who have established cardiovascular disease but without a history of previous myocardial infarction or stroke
<b>Comparators</b>	Established clinical management for the prevention of cardiovascular disease without ticagrelor
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• non-fatal myocardial infarction (STEMI and NSTEMI)</li> <li>• non-fatal stroke</li> <li>• urgent coronary revascularisation</li> <li>• bleeding events</li> <li>• mortality</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life</li> </ul>

<p><b>Economic analysis</b></p>	<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>The use and costs of reversal agents for ticagrelor should be considered in the modelling.</p>
<p><b>Other considerations</b></p>	<p>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.</p>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p><b>Related Technology Appraisals:</b></p> <p>‘Cardiovascular events (reducing, high risk) – ticagrelor’ (2016) NICE technology appraisal ID813. Review date December 2019</p> <p><b>Technology appraisals in development:</b></p> <p>Rivaroxaban for preventing major cardiovascular events in people with coronary or peripheral artery disease. Proposed NICE technology appraisal ID1397. Publication date to be confirmed.</p> <p><b>Suspended technology appraisals:</b></p> <p>Empagliflozin for reducing the risk of death from cardiovascular disease in people with type 2 diabetes Proposed NICE technology appraisal ID1037.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">‘Type 2 diabetes in adults: management’</a> (2015). NICE guideline 28. Updated May 2018.</p> <p><a href="#">‘Cardiovascular disease: risk assessment and reduction, including lipid modification’</a> (2014). Clinical guideline 181. Review date 2018.</p> <p><a href="#">‘Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease’</a> (2013). Clinical guideline 172. Published 2013</p>

	<p><b>Related Public Health Guidance/Guidelines:</b></p> <p><a href="#">‘Cardiovascular disease prevention’</a> (2010) NICE public health guideline 25.</p> <p><a href="#">Chest pain of recent onset: assessment and diagnosis</a> (2010) NICE guideline CG95</p> <p><a href="#">‘Cardiovascular disease: identifying and supporting people most at risk of dying early’</a> (2008) NICE public health guideline 15</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">‘Diabetes in adults’</a> (2011). NICE quality standard 6.</p> <p><a href="#">‘Cardiovascular risk assessment and lipid modification’</a> (2015) NICE quality standard 100</p> <p><a href="#">Secondary prevention after a myocardial infarction</a> (2015) NICE quality standard 99</p> <p><a href="#">Stable angina</a> (2012) NICE quality standard 21</p> <p><b>Related NICE Pathways:</b></p> <p><a href="#">Cardiovascular disease prevention</a> (2018) NICE pathway</p> <p><a href="#">Chest pain</a> (2017) NICE pathway</p> <p><a href="#">Cardiovascular disease: identifying and supporting people most at risk of dying early</a> (2017) NICE pathway</p> <p><a href="#">Myocardial infarction: rehabilitation and preventing further cardiovascular disease</a> (2017) NICE pathway</p> <p><a href="#">Diabetes</a> (2018) NICE pathway</p> <p><a href="#">Type 2 diabetes in adults</a> (2018) NICE pathway</p>
<p><b>Related National Policy</b></p>	<p>Department of Health (2016) ‘NHS Outcomes Framework 2015-2016’. Domains 1 to 5. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a>.</p> <p>NHS England (2016) ‘Manual for Prescribed Specialist Services’. Chapter 67. <a href="https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf">https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</a></p> <p>NHS England (2014) Action on diabetes <a href="https://www.england.nhs.uk/wp-content/uploads/2014/01/act-for-diabetes.pdf">https://www.england.nhs.uk/wp-content/uploads/2014/01/act-for-diabetes.pdf</a></p>

### Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for preventing cardiovascular events in people with type 2 diabetes and coronary artery disease?

- Would people with type 2 diabetes and coronary artery disease be treated with anticoagulation or antiplatelet therapy for secondary prevention of cardiovascular events? If so, which antiplatelet treatments would be used?
- Would lipid modification therapy be used as a treatment for preventing cardiovascular events in people with type 2 diabetes and coronary artery disease?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom ticagrelor is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider ticagrelor will fit into the existing NICE pathways, [Type 2 diabetes in adults](#) and [cardiovascular disease prevention](#)?

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.

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>).

### References

1. Diabetes UK. [Diabetes Prevalence](#), November 2017. (Accessed September 2018)
2. Diabetes.co.uk *Diabetes and Heart Disease*. Available from: <https://www.diabetes.co.uk/diabetes-complications/heart-disease.html> [Accessed 19th June 2018]