Appendix A

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Ticagrelor for the treatment of acute coronary syndromes

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ticagrelor, within its licensed indication, for the treatment of acute coronary syndromes.

Background

The term acute coronary syndrome (ACS) is used to refer to a group of clinical symptoms associated with acute myocardial ischaemia. It encompasses a spectrum of disorders including acute myocardial infarction (MI) and unstable angina pectoris. ACS is usually the result of an acute or sub-acute primary reduction of myocardial oxygen supply provoked by disruption of an atherosclerotic plaque (build-up of fat and other substances in the lining of the artery wall) associated with inflammation, thrombosis, vasoconstriction and microembolisation. In 2006/7 there were 70,000 cases of unstable angina, and 113,000 cases of acute MI with 24,000 subsequent MIs in the UK. ACS becomes more common with increasing age and incidence is higher in men than women.

The presence of persistent ST-segment-elevation on an electrocardiogram usually indicates total occlusion of the affected artery, resulting in necrosis of the tissue supplied by that artery (acute MI). This condition (STEMI) is treated immediately with reperfusion therapy (thrombolysis or percutaneous coronary intervention [PCI]). ACS without ST-segment-elevation is classified as either unstable angina or non-ST-segment-elevation myocardial infarction (NSTEMI). NSTEMI differs from unstable angina primarily in the severity of myocardial ischaemia. In NSTEMI, the ischaemia is severe enough to result in the release of biochemical markers of myocardial injury into the blood. Immediate treatment for these conditions aims to prevent progression to total occlusion of the artery and, for people at high risk of MI, may include a revascularisation procedure, either by means of PCI or coronary artery bypass graft.

NICE has recommended prasugrel (Technology Appraisal No.182) as an option for preventing atherothrombotic events in people with ACS having PCI, only when immediate primary PCI for STEMI is necessary, or stent thrombosis has occurred during clopidogrel treatment, or the patient has diabetes mellitus. NICE has also produced a clinical guideline (Clinical Guideline 94) on unstable angina and NSTEMI which has updated and replaced guidance on clopidogrel (Technology Appraisal No.80) and glycoprotein IIb/IIIa inhibitors (Technology Appraisal No.12 and No. 47). The guideline recommends that:

- aspirin should be offered as soon as possible to all patients and continued indefinitely unless contraindicated by bleeding risk or aspirin hypersensitivity. For patients with hypersensitivity to aspirin, clopidogrel monotherapy should be considered as an alternative.
- for people with increased risk of mortality and no contraindications or for all patients with no contraindications who may undergo PCI within 24 hours of hospital admission, clopidogrel in combination with low-dose aspirin for 12 months after the most recent acute episode of NSTEMI ACS is recommended. Thereafter, standard care, including treatment with low-dose aspirin alone is recommended.

The technology

Ticagrelor (Brilinta, Astrazeneca) belongs to a class of drugs called cyclopentyltriazolopyrimidine inhibitors (ATP analogues). It is an oral, reversibly bound antagonist of the P2Y 12 adenosine diphosphate (ADP) receptor which inhibits platelet aggregation.

Ticagrelor is not currently licensed in the UK for the treatment of ACS. It has been studied in clinical trials in combination with aspirin versus clopidogrel in combination with aspirin in people with ACS, some of whom had undergone revascularisation in the past.

Intervention(s)	Ticagrelor plus aspirin
Population(s)	Patients presenting with ACS irrespective of whether they have undergone revascularisation.
Standard comparators	For people who are to be managed with PCI: • clopidogrel plus aspirin • prasugrel plus aspirin For people who are not to be managed with PCI: • clopidogrel plus aspirin
Outcomes	The outcome measures to be considered include: • mortality • thrombotic cardiovascular events • need for revascularlisation • 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	If the evidence allows the following subgroups will be considered: people with unstable angina, NSTEMI, and STEMI. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. TA80, July 2004, Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome. Review updated and replaced by guideline 94 'Unstable angina and non ST elevation myocardial infarction'. Technology Appraisal No. TA47, September 2002, Glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes. Review partially updated by guideline 94 'Unstable angina and NSTEMI'. Technology Appraisal No. TA 182, October 2009, Prasugrel for the treatment acute coronary artery syndromes with percutaneous coronary intervention. Related Guidelines: Clinical Guideline No. CG48, May 2007, Secondary prevention in primary and secondary care for patients following a myocardial infarction. Review date May 2010. Clinical Guideline No. CG94, March 2010, The management of unstable angina and non ST elevation myocardial infarction.