NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Vorapaxar for the secondary prevention of atherothrombotic events after myocardial infarction

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of vorapaxar within its licensed indication for the prevention of atherothrombotic events in people who have had a prior myocardial infarction.

Background

Atherosclerosis is the build-up of fatty material in artery walls to form a plaque causing narrowing of the artery and disrupted blood flow. If the plaque ruptures a thrombus (blood clot) can form, embolise (travel in the blood stream) and may block blood flow to the heart causing a myocardial infarction or block blood flow to the brain causing a stroke.

In 2011/12 there were approximately 80,000 hospital admissions with myocardial infarction in England and Wales. The most common cause of myocardial infarction is coronary heart disease resulting from atherothrombosis in the coronary arteries. Risk factors for coronary heart disease include smoking, a diet high in saturated fat, high blood pressure, diabetes, being overweight or obese, lack of exercise, age and gender and a family history.

NICE clinical guideline 48 for the secondary prevention in primary and secondary care for patients following a myocardial infarction recommends exercise, dietary changes and help to stop smoking for people who smoke. It also recommends that all patients who have an acute myocardial infarction should be offered treatment with a combination of an angiotensin-converting enzyme inhibitor, aspirin, a beta-blocker and a statin. For patients who have had an acute myocardial infarction and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist is recommended.

Some people may receive treatment with dual antiplatelet therapy following a myocardial infarction (aspirin either with clopidogrel, prasugrel or with ticagrelor) and for continued secondary prevention. NICE clinical guideline 48 recommends that, following a ST-segment-elevation myocardial infarction, patients should receive treatment with a combination of clopidogrel for 4 weeks followed by low-dose aspirin, unless there are other indications to continue dual antiplatelet therapy. People with non-ST-segment-elevation acute coronary syndrome should receive treatment for 12 months with clopidogrel with aspirin followed by low-dose aspirin only unless there are

other indications to continue dual antiplatelet therapy. Following on from the recommendations in NICE clinical guideline 48, technology appraisal 210 recommends clopidogrel for the prevention of ongoing vascular events as an option for people who have had a myocardial infarction if aspirin is contraindicated or not tolerated.

Technology appraisal 182 recommends prasugrel in combination with aspirin for preventing atherothrombotic events in people with acute coronary syndromes having percutaneous coronary intervention for ST segment elevation, only when: immediate primary percutaneous coronary intervention for ST segment elevation myocardial infarction is necessary or stent thrombosis has occurred during clopidogrel treatment or the patient has diabetes mellitus. The guidance recommends that prasugrel can be used for up to 12 months. Technology appraisal 236 recommends ticagrelor in combination with low-dose aspirin for up to 12 months as a treatment option for people with ST-segment-elevation myocardial infarction (STEMI) that cardiologists intend to treat with primary percutaneous coronary intervention (PCI) or non-ST-segment-elevation myocardial infarction and some people with unstable angina. Guidance from Technology Appraisal 236 has now been incorporated into NICE Clinical Guideline 167 Myocardial infarction with ST-Segment elevation.

The technology

Vorapaxar (Brand name unknown, Merck) is an inhibitor of protease-activated receptor 1 (PAR-1). It inhibits thrombin-associated activation of platelets, without activating the clotting cascade. It is administered orally.

Vorapaxar does not have a UK marketing authorisation. It has been studied in a clinical trial as an add-on to standard care (e.g. aspirin, clopidogrel) for people with a history of atherosclerosis compared to standard care alone for the prevention of heart attack and stroke.

Intervention(s)	Vorapaxar with standard care including aspirin with or without clopidogrel
Population(s)	People who have had a prior myocardial infarction
Comparators	• standard care including antiplatelet treatment with aspirin alone or aspirin with clopidogrel • standard care including antiplatelet treatment with aspirin and prasugrel (for people for whom prasugrel is recommended) • standard care including antiplatelet treatment with aspirin with ticagrelor (for people for whom ticagrelor is recommended)

Outcomes	The outcome measures to be considered include: • myocardial infarction • stroke • recurrent ischaemia leading to urgent coronary vascularisation • 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.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 182, Oct 2009, 'Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention'. Under review. Technology Appraisal No. 210, Dec 2010, 'Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (review of technology appraisal guidance 90)'. Review proposal date July 2013. Technology Appraisal No. 230, Jul 2011, 'Bivalirudin for the treatment of ST-segment-elevation myocardial infarction' On static list Technology Appraisal No. 236, Oct 2011 'Ticagrelor for the treatment of acute coronary syndromes'. Currently under consideration for review. Technology Appraisal in Preparation, 'Rivaroxaban for the prevention of adverse outcomes in patients after the acute management of acute coronary syndrome'. Earliest anticipated date of publication Mar 2015.

	Related Clinical Guidelines: Clinical Guideline No. 48, May 2007 'Secondary prevention in primary and secondary care for patients following a myocardial infarction'. Currently under review, earliest anticipated publication date Nov 2013. Clinical Guideline No. 94, Mar 2010 'Unstable angina and NSTEMI: the early management of unstable angina and non-ST-segment-elevation myocardial infarction'. Clinical Guideline No. 95, Mar 2010 'Chest pain of recent onset: Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. Clinical Guideline No. 167, July 2013, 'Myocardial infarction with ST-segment elevation: The acute management of myocardial infarction with ST-segment elevation'. Related Public Health Guidelines: Public Health Guideline No. 25, June 2010 'Prevention of cardiovascular disease'. Next review date December 2015. Related Quality Standards: Quality Standard No. 9, Jun 2011 'Chronic heart failure' http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Chronic heart failure Pathway created Jan 2013 NICE Pathway: Acute Coronary Syndrome. Pathway created July 2013 http://pathways.nice.org.uk/
Related NHS England Policy	Manual for prescribed specialised services, November 2012, Chapter 8 Adult specialist cardiac service. http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf

Questions for consultation

Have the most appropriate comparators for vorapaxar for the secondary prevention of cardiovascular events been included in the scope?

- Are the comparators listed routinely used in clinical practice?
- Would vorapaxar be added to prasugrel with aspirin or ticagrelor with aspirin for people receiving ongoing treatment with these antiplatelet drugs following myocardial infarction?

How soon after an acute myocardial infarction would treatment with vorapaxar commence? What is the expected duration of treatment with vorapaxar?

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

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 vorapaxar 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 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)

Subject to referral by the Department of Health, the invite for participation in this technology appraisal is anticipated for after January 2014, when new arrangements for the pricing of pharmaceuticals are expected to be in place. Consequences for this appraisal will be explored through further consultation on the scope pre-invitation.