Prasugrel for the treatment of acute coronary artery syndromes with percutaneous coronary intervention

J Greenhalgh,* A Bagust, A Boland, CM Saborido, N Fleeman, C McLeod, Y Dundar, R Dickson, C Proudlove, R Kolamunnage-Dona and M Fisher

Liverpool Reviews and Implementation Group, University of Liverpool, Liverpool, UK

*Corresponding author

Declared competing interests of authors: Michael Fisher has received remuneration from Bristol Myers Squibb/Sanofi for consultancy, symposium attendance, organising education, speaking and staffing.

Abstract

This paper presents a summary of the evidence review group (ERG) report into the clinical effectiveness and cost-effectiveness of prasugrel for the treatment of coronary artery syndromes with percutaneous coronary intervention, based upon the evidence submission from Eli Lilly to the National Institute for Health and Clinical Excellence (NICE) as part of the single technology appraisal process. The submitted clinical evidence was based on a phase III double-blind, double-dummy randomised controlled trial which compared the use of prasugrel with clopidogrel. The primary clinical outcome measure was a composite end point of death from cardiovascular causes, non-fatal myocardial infarction (MI) or non-fatal stroke at 15 months. Secondary outcomes included the primary end point at 30 days and 90 days; a composite end point of death from cardiovascular causes, non-fatal MI or urgent target vessel revascularisation; a composite end point of death from cardiovascular causes, non-fatal MI, non-fatal stroke or rehospitalisation due to a cardiac ischaemic event; and stent thrombosis. For the overall trial cohort during the 15 month follow-up period, the results of the trial demonstrated a statistically significant benefit of prasugrel compared with clopidogrel on the primary outcome. The efficacy difference between treatment groups was, in the main, due to a statistically significant lower incidence of non-fatal

HTA 08/78/01

Date of ERG submission:
April 2009

TAR Centre(s):
Liverpool Reviews and Implementation Group (LRiG)

List of authors:
J Greenhalgh, A Bagust, A Boland, CM Saborido, N Fleeman, C McLeod, Y Dundar, R Dickson, C Proudlove, R Kolamunnage-Dona and M Fisher

Contact details:
Janette Greenhalgh, Liverpool Reviews and Implementation Group (LRiG), University of Liverpool, Room BO5 Whelan Building, The Quadrangle, Brownlow Hill, Liverpool L69 3GB, UK

E-mail: janette.greenhalgh@liverpool.ac.uk

The research reported in this article of the journal supplement was commissioned and funded by the HTA programme on behalf of NICE as project number 08/78/01. The assessment report began editorial review in May 2009 and was accepted for publication in August 2009 See the HTA programme website for further project information (www.hta.ac.uk). This summary of the ERG report was compiled after the Appraisal Committee's review.

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Department of Health.

Discussion of ERG reports is invited. Visit the HTA website correspondence forum (www.hta.ac.uk/correspond).

MIs in the prasugrel group than in the clopidogrel group. No statistically significant differences were found for death from cardiovascular causes or non-fatal stroke. For the fully licensed and target populations, there was a statistically significant lower incidence of non-fatal MIs in the prasugrel group than in the clopidogrel group; there was no statistically significant difference in bleeding rates. The ERG recalculated the base-case cost-effectiveness results taking changes in parameters and assumptions into account: for example, revised drug costs, mid-cycle correction, amended relative risk mortality. Subgroup and threshold analyses were also explored by the ERG. For the fully licensed population (i.e. excluding patients with prior stroke or TIA), the manufacturer reported an incremental cost-effectiveness ratio (ICER) of £159,358 per quality-adjusted life-year (QALY) gained at 12 months and an ICER of £3,220 per QALY gained at 40 years. Considering the 15-month clinical trial data available for the fully licensed and target populations and current practice in England and Wales, the evidence was considered insufficient to support the conclusion that prasugrel is clinically more effective than clopidogrel or vice versa. Assuming that there is no evidence to distinguish between prasugrel and clopidogrel in terms of clinical effectiveness in the short term for this population, equipoise between prasugrel and clopidogrel at year 1 is achieved by a 20% reduction in the acquisition cost of prasugrel (approximately £120 per patient). At the time of writing, the guidance/has not yet been published by NICE.

Introduction

The National Institute for Health and Clinical Excellence (NICE) is an independent organisation within the NHS that is responsible for providing national guidance on the treatment and care of people using the NHS in England and Wales. One of the responsibilities of NICE is to provide guidance to the NHS on the use of selected new and established health technologies based on an appraisal of those technologies.

NICE's single technology appraisal (STA) process is specifically designed for the appraisal of a single product, device or other technology, with a single indication, where most of the relevant evidence lies with one manufacturer or sponsor.[1] Typically, it is used for new pharmaceutical products close to launch. The principal evidence for an STA is derived from a submission by the manufacturer/sponsor of the technology. In addition, a report reviewing the evidence submission is submitted by the evidence review group (ERG), an external organisation independent of NICE. This paper presents a summary of the ERG report for the STA entitled 'Prasugrel for the treatment of coronary artery syndromes with percutaneous coronary intervention'.[2]

Description of the underlying health problem

Acute coronary syndromes (ACS) are life threatening conditions comprising clinical symptoms associated with acute myocardial ischaemia with or without infarction.[3] ACS represent manifestations of atherosclerosis, which is usually precipitated by acute thrombosis, induced by a ruptured or eroded atherosclerotic plaque, with or without concomitant vasoconstriction, causing a sudden and critical reduction in coronary blood flow.[4]

The leading symptom that initiates the diagnostic and therapeutic cascade is chest pain, but the classification of patients is based on the presentation electrocardiogram.[4] The presence of acute chest pain and persistent ST-segment elevation indicates total occlusion of an affected coronary artery. Most of these patients will ultimately develop ST-segment elevated myocardial infarction (STEMI), resulting in necrosis of the tissue supplied by that artery. ACS with acute pain without ST-segment elevation is classified as either unstable angina (UA) or non-ST-segment elevation myocardial infarction (NSTEMI).[4]

Options for the initial management of ACS patients include: (1) drug therapy (heparin, antiplatelet agents, beta blockers, nitrates, calcium channel blockers, thrombolytic agents and statins) or (2) drug therapy in combination with an early invasive strategy with percutaneous coronary intervention (PCI) (with or without coronary stenting) or coronary artery bypass grafting (CABG). PCI with coronary stenting is endorsed as an early invasive treatment for intermediate to high risk patients with ACS.[4,5]

Approximately 15% of the UK ACS population is treated with PCI. In 2007, within the 250,000 patients diagnosed with ACS, 77,373 PCIs were performed. Of these, 40.48% were patients with UA/NSTEMI and 13.24% were patients with STEMI. Most of the remaining patients (45.10%) had stable disease.[6]

Scope of the evidence review group report

Prasugrel is licensed in Europe to be co-administered with aspirin for the prevention of atherothrombotic events in patients with ACS undergoing primary or delayed PCI. The use of prasugrel in patients with a history of stroke or transitory ischaemic attack (TIA) is contraindicated in the Special Product Characteristics, whilst use of prasugrel in lighter (less than 60 kg) and older (75 years or more) patients is generally not recommended.

The ERG report presents the results of the evaluation of the manufacturer (Eli Lilly) evidence submission regarding the use of prasugrel with patients with ACS who are to be managed with PCI. The report includes an assessment of both the clinical effectiveness and cost-effectiveness evidence submitted by the manufacturer. The manufacturer submission described the use of prasugrel in combination with aspirin compared with clopidogrel in combination with aspirin.

The primary clinical outcome measure was a composite end point of death from cardiovascular causes, non-fatal myocardial infarction (MI) or non-fatal stroke at 15 months. Secondary outcomes included the primary end point at 30 days and 90 days; a composite end point of death from cardiovascular causes, non-fatal MI or urgent target vessel revascularisation; a composite end point of death from cardiovascular causes, non-fatal MI, non-fatal stroke or rehospitalisation due to a cardiac ischaemic event; and stent thrombosis. Safety end points included non-CABG-related thrombolysis in MI (TIMI) major bleeding, TIMI life threatening and TIMI minor bleeding. Health-related quality of life (HRQoL) was also measured.

An additional outcome measure of net clinical benefit comprising a composite end point of death from any cause, non-fatal MI, non-fatal stroke, or non-CABG-related non-fatal TIMI major bleeding was calculated.

Cost-effectiveness was measured in terms of incremental cost-effectiveness ratios (ICERs) per quality-adjusted life-year (QALY) gained.

Data for a number of different patient populations were presented:

- overall trial cohort including stroke or TIA ($n = 13,608$)
- all the ACS licensed population excluding prior stroke or TIA ($n = 13,090$)
- ACS 10-mg licensed population excluding prior stroke or TIA (target population) ($n = 10,941$)
- UA/NSTEMI licensed population excluding prior stroke or TIA ($n = 9669$)
- STEMI licensed population excluding prior stroke or TIA ($n = 3421$)
- ACS licensed population excluding prior stroke or TIA with diabetes ($n = 2947$)
- ACS licensed population excluding prior stroke or TIA without diabetes ($n = 10,143$).

Methods

The ERG report comprised a critical review of the evidence for the clinical effectiveness and cost-effectiveness of the technology based upon the manufacturer's submission to NICE as part of the STA process.

The ERG evaluated the quality of the manufacturer's clinical effectiveness review. Searches conducted by the manufacturer were assessed for completeness, and the single trial put forward as evidence of effectiveness was critically appraised using the manufacturer's responses to specific questions in the submission template. With regard to cost-effectiveness evidence, the ERG assessed the manufacturer's searches for completeness, critically appraised the submitted economic model using a standard assessment tool[7] and conducted a detailed evaluation of the model. The ERG recalculated the base-case cost-effectiveness results taking changes in parameters and assumptions into account: for example, revised drug costs, mid-cycle correction, amended relative risk mortality. Subgroup and threshold analyses were also explored by the ERG.

Results

Summary of submitted clinical evidence

The clinical effectiveness evidence was derived from a phase III double-blind, double-dummy randomised controlled trial (RCT) which compared the use of prasugrel with clopidogrel. The TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel (TRITON)–TIMI 38 was conducted in 30 countries and included 13,608 patients. For the overall trial cohort during the 15 month follow-

up period, the results of the TRITON–TIMI 38 trial demonstrated a statistically significant benefit of prasugrel compared with clopidogrel on the primary outcome (a composite end point of death from cardiovascular causes, non-fatal MI or non-fatal stroke). The efficacy difference between treatment groups was, in the main, due to a statistically significant lower incidence of non-fatal MIs in the prasugrel group than in the clopidogrel group. No statistically significant differences were found for death from cardiovascular causes or non-fatal stroke. The trial results reported a benefit for prasugrel in the overall trial cohort for the majority of secondary end points with the exception of death from any cause, where no statistical difference was identified. The results are summarised in *Table 1*. In the trial, HRQoL data were limited as this substudy comprised responses from too few patients. In the overall trial cohort, statistically significantly more bleeding events occurred in patients in the prasugrel arm than in those in the clopidogrel arm. The analysis of the pre-specified net clinical benefit outcome (death from any cause, non-fatal MI, non-fatal stroke, or non-CABG-related non-fatal TIMI major bleeding) favoured the use of prasugrel in the overall trial cohort. For the fully licensed and target populations, there was a statistically significant lower incidence of non-fatal MIs in the prasugrel group than in the clopidogrel group; there was no statistically significant difference in bleeding rates.

Summary of submitted cost-effectiveness evidence

In the absence of UK-based economic evaluations of prasugrel for patients with ACS undergoing PCI, the manufacturer conducted a de novo economic evaluation. The analysis described in the manufacturer submission used a Markov model structure with cohorts of patients modelled to experience events over the course of the TRITON–TIMI 38 study period with long-term mortality based on adjustment of population life tables

TABLE 1 *TRITON–TIMI 38: Efficacy results at 15 months (overall cohort)*

End point	Prasugrel (*n* = 6813) *n* (%)	Clopidogrel (*n* = 6795) *n* (%)	HR (95% CI)	*p*-value[a]
Primary				
Death from CV causes, non-fatal MI or nonfatal stroke	643 (9.9)	781 (12.1)	0.81 (0.73 to 0.90)	< 0.001
Death from CV causes	133 (2.1)	150 (2.4)	0.89 (0.70 to 1.12)	0.31
Non-fatal MI	475 (7.3)	620 (9.5)	0.76 (0.67 to 0.85)	< 0.001
Non-fatal stroke	61 (1.0)	60 (1.0)	1.02 (0.71 to 1.45)	0.93
Secondary				
Death from any cause	188 (3.0)	197 (3.2)	0.95 (0.78 to 1.16)	0.64
Death from CV causes, nonfatal MI or UTVR	652 (10.0)	798 (12.3)	0.81 (0.73 to 0.89)	< 0.001
Death from CV causes	133 (2.1)	150 (2.4)	0.89 (0.70 to 1.12)	0.31
Non-fatal MI	475 (7.3)	620 (9.5)	0.76 (0.67 to 0.85)	< 0.001
UTVR[b]	156 (2.5)	233 (3.7)	0.66 (0.54 to 0.81)	< 0.001
Stent thrombosis[c]	68 (1.1)	142 (2.4)	0.48 (0.36 to 0.64)	< 0.001
Death from CV causes, nonfatal MI, non-fatal stroke or rehospitalisation for ischaemia	797 (12.3)	938 (14.6)	0.84 (0.76 to 0.92)	< 0.001

CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction; UTVR, urgent target vessel revascularisation.

a *p*-values were calculated using the log-rank test. The analysis for the primary end point used the Gehan–Wilcoxon test for which the *p*-value was less than 0.

b Taken from published paper.[8]

c Stent thrombosis defined as definite or probable according to the Academic Research Consortium.

to reflect prognostic implications of the events modelled over the short term. The model also permitted in-hospital costs to accumulate after the end of the trial follow-up period. The model can be separated into two distinct phases: (1) the trial-based period of 15 months and (2) extrapolation beyond the trial to a lifetime horizon (40 years). The economic evaluation adopts a lifetime horizon for the consideration of in-hospital costs and benefits and the perspective is that of the UK NHS and Personal Social Services.

For the fully licensed population (i.e. excluding patients with prior stroke or TIA), the manufacturer reported an ICER of £159,358 per QALY gained at 12 months and an ICER of £3,220 per QALY gained at 40 years; the incremental QALY gain for prasugrel patients is very small (0.001 QALYs and 0.05 QALYs at 12 months and 40 years respectively). In addition to the main results, ICERs for selected subgroups were also presented at 40 years. Univariate sensitivity analysis was undertaken using a range of parameters. At 40 years, using the median UA/NSTEMI profile and halving the relative risks for all-cause mortality increases the ICER to £10,070 per QALY gained; varying the relative risk for prasugrel compared with clopidogrel in the first 3 days in an attempt to explore the preloading of clopidogrel on cost-effectiveness yielded a maximum ICER for this median patient profile of £22,727 per QALY gained.

Probabilistic sensitivity analysis was also conducted by the manufacturer using median patient profiles. At 40 years, the probabilistic sensitivity analyses illustrate that prasugrel is likely to be cost-effective compared with clopidogrel (around 75%) for what would usually be considered low levels of willingness to pay (£20,000) for an additional QALY; the ICERs were within the cost-effectiveness threshold range used by NICE.

Commentary on the robustness of submitted evidence

The manufacturer cited evidence from a large trial (TRITON–TIMI 38) to support the superior clinical effectiveness of prasugrel compared with clopidogrel for the treatment of patients with ACS managed with PCI. The trial used robust randomisation techniques and was suitably powered to show a clinical difference in the primary efficacy composite end point between the treatment groups. Appropriate pre-specified subgroup analyses and post hoc exploratory analyses were carried out.

There is only one relevant RCT (TRITON–TIMI 38) that compares prasugrel versus clopidogrel with PCI. The clinical superiority of prasugrel over clopidogrel on the primary efficacy endpoint is driven largely by a reduction in non-fatal MI, an event recorded clinically (symptomatic) and non-clinically (by biomarkers/electrocardiogram readings). If the non-clinical MIs were considered less important to patients, the resultant clinical difference in non-fatal MIs alone may not be statistically significant.

The primary efficacy composite end point used in the trial may not be appropriate as it fails to meet published recommendations. In addition, there is limited generalisability of the trial protocol to NHS patients in England and Wales due to differences in the use of clopidogrel and its current use in UK clinical practice. Moreover, the growing trend in England and Wales for PCI to be performed via radial artery access is not reflected in the trial; there is evidence that when PCI is performed radially, major bleeding rates are reduced. The HRQoL trial data were limited as the quality of life substudy recruited too few patients to allow meaningful analysis of responses.

The economic model described in the manufacturer submission made use of a large quantity of individual patient data allowing the heterogeneity of different patient groups to be assessed. The manufacturer asked a clearly defined question and attempted to identify, measure and value relevant costs and benefits in the economic evaluation.

The ERG identified six key areas where corrections and/or adjustments to the economic model were required: life table calculations to allow for competing risks; conventional approach to discounting; revised treatment costs reflecting actual usage and pack wastage; alternate utility values; amended long-term relative risks of mortality; and reduced incidence of non-fatal recurrent MIs. Taken together, these corrections and/or adjustments have increased the size of the ICER for all patient populations (*Table 2*).

The methods used to project outcomes and costs after the trial period are crucial to the acceptance or rejection of the manufacturer's ICER. The ERG advises caution in view of the various problems that are apparent with this part of the submitted model. If the ERG had been able to modify some of the model's underlying assumptions, then it is likely that the magnitude of the re-estimated ICER would be increased further.

TABLE 2 *Cost-effectiveness from submitted model[a] and with ERG modifications[a]*

Population	Model version	Horizon	Clopidogrel			Prasugrel			Incremental			ICERs	
			LYs	QALYs	Costs	LYs	QALYs	Costs	LYs	QALYs	Costs	£ per LY	£ per QALY
ACS	Submitted	1 year	0.97	0.720	£874	0.97	0.720	£1032	–0.0002	–0.0002	£158.40	clop dom	clop dom
		10 years	7.95	6.126	£3342	7.95	6.129	£3500	0.0036	0.0027	£157.67	£44,405	£57,641
		40 years	14.30	10.960	£5574	14.34	10.990	£5744	0.0392	0.0296	£170.18	£4346	£5751
	ERG	1 year	0.99	0.646	£860	0.99	0.646	£1031	–0.0001	–0.0001	£120.07	clop dom	clop dom
		10 years	8.11	5.459	£3372	8.11	5.459	£3543	–0.0002	–0.0002	£119.85	clop dom	clop dom
		40 years	14.69	9.770	£5685	14.70	9.776	£5859	0.0093	0.0060	£123.19	£13,294	£20,475
UA/NSTEMI	Submitted	1 year	0.97	0.778	£873	0.97	0.778	£1031	–0.0003	–0.0002	£158.50	clop dom	clop dom
		10 years	8.12	6.378	£3404	8.13	6.378	£3560	0.0007	0.0005	£156.84	£235,284	£340,331
		40 years	16.37	12.701	£6299	16.40	12.728	£6468	0.0349	0.0265	£168.88	£4832	£6382
	ERG	1 year	0.99	0.663	£859	0.99	0.663	£1031	–0.0002	–0.0002	£120.72	clop dom	clop dom
		10 years	8.28	5.695	£3431	8.28	5.694	£3602	–0.0014	–0.0010	£120.15	clop dom	clop dom
		40 years	16.79	11.324	£6423	16.80	11.328	£6597	0.0066	0.0042	£122.95	£18,643	£28,971
STEMI	Submitted	1 year	0.97	0.720	£859	0.97	0.720	£1019	–0.0001	–0.0001	£160.55	clop dom	clop dom
		10 years	7.88	6.074	£3300	7.88	6.077	£3461	0.0037	0.0029	£160.65	£43,258	£56,032
		40 years	13.63	10.431	£5321	13.67	10.455	£5492	0.0319	0.0241	£170.56	£5347	£7087
	ERG	1 year	0.99	0.646	£850	0.99	0.646	£1021	–0.0001	–0.0001	£118.58	clop dom	clop dom
		10 years	8.04	5.362	£3335	8.04	5.362	£3507	0.0001	0.0000	£118.86	£2,332,985	£18,536,759
		40 years	13.97	9.242	£5419	13.98	9.247	£5593	0.0077	0.0050	£121.56	£15,695	£24,161

Population	Model version	Horizon	Clopidogrel			Prasugrel			Incremental			ICERs	
			LYs	QALYs	Costs	LYs	QALYs	Costs	LYs	QALYs	Costs	£ per LY	£ per QALY
Diabetes	Submitted	1 year	0.97	0.714	£905	0.97	0.716	£1040	0.0023	0.0017	£135.79	£58,275	£79,531
		10 years	8.01	6.172	£3405	8.04	6.198	£3550	0.0335	0.0259	£144.38	£4304	£5564
		40 years	15.90	12.189	£6178	16.04	12.296	£6360	0.1412	0.1074	£182.19	£1291	£1697
	ERG	1 year	0.98	0.641	£878	0.99	0.642	£1034	0.0025	0.0016	£104.19	£41,490	£63,957
		10 years	8.16	5.539	£3417	8.19	5.559	£3581	0.0302	0.0205	£113.35	£3753	£5517
		40 years	16.34	10.896	£6289	16.42	10.952	£6473	0.0838	0.0556	£132.19	£1577	£2376
Non-diabetes	Submitted	1 year	0.97	0.718	£872	0.97	0.718	£1031	–0.0004	–0.0003	£158.46	clop dom	clop dom
		10 years	7.53	5.706	£3194	7.54	5.711	£3353	0.0066	0.0049	£158.84	£24,246	£32,551
		40 years	11.31	8.528	£4522	11.35	8.555	£4691	0.0356	0.0266	£169.04	£4751	£6365
	ERG	1 year	0.99	0.614	£859	0.99	0.613	£1030	–0.0003	–0.0002	£120.06	clop dom	clop dom
		10 years	7.70	5.003	£3228	7.70	5.002	£3399	–0.0006	–0.0004	£119.77	clop dom	clop dom
		40 years	11.62	7.555	£4604	11.63	7.560	£4778	0.0073	0.0048	£122.54	£16,725	£25,716
Target	Submitted	1 year	0.97	0.720	£873	0.97	0.720	£1032	–0.0002	–0.0002	£158.36	clop dom	clop dom
		10 years	7.91	6.094	£3328	7.91	6.097	£3485	0.0040	0.0031	£157.79	£39,469	£51,185
		40 years	13.93	10.669	£5444	13.97	10.699	£5615	0.0393	0.0297	£170.21	£4326	£5729
	ERG	1 year	0.99	0.646	£860	0.99	0.646	£1031	–0.0002	–0.0001	£120.03	clop dom	clop dom
		10 years	8.07	5.408	£3358	8.07	5.408	£3529	–0.0001	–0.0001	£119.84	clop dom	clop dom
		40 years	14.32	9.496	£5552	14.32	9.502	£5727	0.0094	0.0061	£123.18	£13,144	£20,247

ACS, acute coronary syndromes; clop dom, clopidogrel dominates prasugrel; ERG, evidence review group; ICERs, incremental cost-effectiveness ratios; LYs, life years; NSTEMI, non-ST-segment elevated myocardial infarction; QALYs, quality-adjusted life-years; STEMI, ST-segment elevated myocardial infarction; UA, unstable angina.

a Figures directly taken from model, not manufacturer submission.

Conclusions

Considering the 15-month clinical trial data available for the fully licensed (i.e. excluding prior stroke or TIA) and target populations (i.e. excluding prior stroke or TIA, and patients weighing less than 60 kg or aged 75 years or older) and current practice in England and Wales, the evidence was considered insufficient to support the conclusion that prasugrel is clinically more effective than clopidogrel or vice versa.

Assuming that there is no evidence to distinguish between prasugrel and clopidogrel in terms of clinical effectiveness in the short term for this population, equipoise between prasugrel and clopidogrel at year 1 is achieved by a 20% reduction in the acquisition cost of prasugrel (approximately £120 per patient).

The modelled net health benefits (QALYs) do not achieve positive gains for prasugrel until more than 10 years' follow-up has elapsed, except for patients with diabetes mellitus. The ERG considered that the submitted evidence from long-term projection (at 40 years) is not sufficiently robust to support the conclusion that prasugrel is more cost-effective than clopidogrel for the fully licensed population.

Given that the trial evidence appears to show that prasugrel and clopidogrel yield similar overall health benefits in the short-term, it could be argued that, at an equivalent net cost per patient, prasugrel might represent a viable alternative.

Summary of NICE guidance issued as a result of the STA

The guidance issued by NICE in October 2009 states that:

1.1 Prasugrel in combination with aspirin is recommended as an option for preventing atherothrombotic events in people with acute coronary syndromes having percutaneous coronary intervention, 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.

1.2 People currently receiving prasugrel for treatment of acute coronary syndromes whose circumstances do not meet the criteria in 1.1 should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

Key references

1. NICE. *Guide to the single technology (STA) process.* 2006. URL: www.nice.org.uk/page.aspx?o=STAprocessguide.

2. Greenhalgh J, Bagust A, Boland A, Martin Saborido C, Fleeman N, McLeod C, *et al*. *Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention: A Single Technology Appraisal.* LRiG: University of Liverpool; 2009.

3. Taylor MJ, Scuffham PA, McCollam PL, Newby D. Acute coronary syndromes in Europe: 1-year costs and outcomes. *Cur Med Res Opin* 2007;**23**:495–503.

4. Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Fernandez-Aviles F, *et al*. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. *Eur Heart J* 2007;**28**:1598–660.

5. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE, Jr, *et al*. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction). *Circulation* 2007;**116**:e148–304.

6. BCIS. *BCIS Audit Returns: Adult Interventional Procedures.* 2007. URL: www.bcis.org.uk/resources/audit/audit2007.

7. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *BMJ* 1996;**313**:275–83.

8. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, *et al*. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2007;**357**:2001–15.