

What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Antiplatelet drug therapy is already a key component to the comprehensive management of vascular disease. This appraisal concludes changes in the prescribing balance between the different antiplatelet agents and their combinations in different presentations of vascular disease. The main change is the recommendation to use clopidogrel first line in patients with multivessel disease and PAD. The appraisal excludes patients with recent revascularisation which are a significant cohort with ischaemic heart disease many of whom will be on aspirin and clopidogrel combined following stenting for STEMI and NSTEMI. Indeed the appraisal does not study this crucial drug combination and further trials on it are due. The significant group of patients with AF and OVE are also excluded where guidance is lacking and clinical decision making complex. With an aging population the application of this appraisal to those above the trial ages is also unclear. The issue of clopidogrel resistance separate from proton pump inhibitor prescribing is of increasing concern especially in the STEMI group and not fully covered, nor indeed is aspirin resistance. Finally there are newer antiplatelet agents now marketed or close to marketing (Prasugrel, Ticagrelor etc) which are not included which may be relevant especially following STEMI and coronary stenting.

This appraisal should support regular antiplatelet prescribing audits in primary and secondary care; both initiation and continuation of therapy. The definition of aspirin intolerance is vague so the balance between aspirin and clopidogrel prescribing when they are first and second line therapy should be studied. The appraisal notes that Clopidogrel is used in TIA outside of licence when other agents are not tolerated even though not licenced. This would be viewed as clinically acceptable but data on its frequency would be interesting.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

This is not new technology just a change in balance of use of existing drug therapy. Real world patients are different to trial patients particularly their age but this is the best data available. The main 'side effect' of increasing the use of more potent antiplatelet agents may be an increase in bleeding risk although the reduction in thrombotic events should be greater. This is more relevant with more potent dual antiplatelet therapy not covered in this appraisal.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

New antiplatelet agents are now available.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

The use of Clopidogrel should increase. Now this is off patent cost rises will be less marked. As dual therapy is common in STEMI and NSTEMI patients outside of this appraisal it will not be the sole cause of increased use.