NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Ivabradine for the treatment of chronic heart failure

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Simon Williams

Name of your organisation
Wythenshawe Hospital, Manchester

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? Yes
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? Yes, previous involvement (investigator) in previous trial, BEAUTIFUL
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? Consultant Cardiologist & Clinical specilaity lead, Wythenshawe Hospital, Manchester
- other? (please specify) N/A

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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?

Therapies are adopted and used in line with NICE clinical guideline 108. There is consensus amongst specialists to up-titrate beta-blockers up to maximum dose as far as possible. However, there is variation in how fully that is implemented in primary care.

There is some geographical variation in the how the services are run, usually led from hospital-based heart failure clinic, but may be stronger community emphasis particularly if HF nurse specialist works there.

There are no alternatives to ivabradine in the relevant patients.

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?

Patients with higher heart rates and higher NYHA class, and the elderly, are at greater risk of events.
Ivabradine has demonstrated efficacy in the overall SHIFT trial, however efficacy increases with baseline heart rate hence licence restricted to patients with heart rate 75 bpm or above. No difference in efficacy is expected across other subgroups.

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)?

Ivabradine should be initiated through heart failure service, which tend to be cardiology led from secondary care, however may also be located in primary care. GPwSI and heart failure nurses may appropriately initiate and titrate ivabradine in some settings. The healthcare professional needs to have the experience to know when beta-blockade has been optimised before considering ivabradine.

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?

Ivabradine is being used within its licensed indication both in the management of heart failure (new indication) and for symptomatic relief of Stable Angina (existing indication).
Many heart failure services are not using ivabradine at all, hence guidance from NICE is needed to ensure appropriate uptake.

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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.

NICE clinical guideline 108 appropriately recommends first line use of beta-blockers and ACE inhibitors, based on the wealth of evidence for these interventions in patients with heart failure due to LVSD.
CG 108 was published prior to the publication of two key studies in heart failure: EMPHASIS (eplerenone) and SHIFT (ivabradine).

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?

Ivabradine is not proposed as an alternative to beta-blockers and is licensed for use on top of standard therapy including optimised beta-blockade. Occasionally, patients have specific tolerability issues with beta-blockers and ivabradine may be appropriate in this group.

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.

Not applicable. Ivabradine is a chronic therapy that will be continued for the lifetime of patients regarded as suitable for the therapy.
Usual assessment of heart failure patients as defined in NICE CG 108 is appropriate with ivabradine and nothing additional is required.

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?

Generalisability: SHIFT patients are slightly younger than observed in clinical practice. This is an issue common to clinical trials generally and it is anticipated that the results would extrapolate well to a UK setting.

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Background therapy in SHIFT may be regarded as optimal for these patients and is expected to approximate well to dosing levels which may be achieved in UK practice.

The primary outcome of SHIFT (mortality and hospitalisation) are amongst the most important outcomes for patients with heart failure. Quality of life is also important, and this is also investigated within the trial.

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?

Phosphenes (visual symptoms) are a recognised side-effect of ivabradine. When they do occur, symptoms resolve in most patients during treatment.

Bradycardia is another recognised adverse reaction, occurring in 3% of patients on treatment. 0.5% of patients are reported in trials as experiencing severe bradycardia (40 beats per minute or less), as described in the SPC.

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.

Not aware of any such information.

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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)?

Assuming positive NICE guidance in line with the licensed indication, delivery of care would be straight forward and no additional education, training, facilities or equipment would be required.
There is sufficient guidance in place already regarding the need to up-titrate beta-blockers to maximum tolerated doses before considering ivabradine.