NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Vemurafenib for the treatment of unresectable locally advanced or metastatic, $BRAF^{V600}$ mutation positive malignant melanoma

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: Dr Louise Fearfield

Name of your organisation: British Association of Dermatologists

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**
- 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)? **Yes**
- other? (please specify)
-

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

How is the condition currently treated in the NHS? **Standard treatment is with Dacarbazine; single agent and not very effective** Is there significant geographical variation in current practice? **Few centres have Vemurafenib available to treat patients as part of clinical trials. Most centres only have Dacarbazine.** Are there differences of opinion between professionals as to what current practice should be? **Most professionals would agree that Vemuraenib should be considered in unresectable BRAF mutation positive melanoma.** What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages? **1.) Dacarbazine; not very effective but well tolerated with minimal side effects. 2.) Ipilumumab (CTLA4 inhibitor) expensive with significant side effects (diarrhoea). Has been shown to be more effective than single agent Dacarbazine. Not mutation defined treatment.**

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? **No** Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology? **Can only use in BRAF positive mutation unresectable melanoma, 40-50% of patients.**

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? **Secondary care, specialist oncology clinics after discussion through a specialist MDT** Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)? **Oncologists, Dermatologist and Specialist cancer nurses needed to oversee treatment.**

If the technology is already available, is there variation in how it is being used in the NHS? **Not available at present.** 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. **Roche have developed guidelines for treatment in the trial setting. I am currently writing a management guideline and management algorithm for the skin toxicities that are associated with vemurafenib. Not as yet published. I have first hand experience in treating over 40 patients with vemurafenib and managing their skin toxicities**

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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? **It will be a very useful first line treatment for BRAF mutation positive unresectable melanoma patients. It is a daily oral treatment so patients do not need to come into hospital for treatment as with Dacarbazine.**

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. **It can only be used for BRAF mutation positive melanoma patients.**

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? **The current clinical trials using vemurafenib reflect how it would be used in clinical practice which would not differ from the trial setting. Overall survival and disease free interval were measured in the trial setting and results have been published so far in the New England medical journal** ***New England Journal of Medicine*****. 364, 26, 2507-2516.**

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?
Main side effects involve the skin and joints. When side effects are severe dose reduction is required. Otherwise less severe side effects can be managed by additional treatments such as topical steroids, emollients for rashes and non-steroidal inflammatories for arthritis.

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. **No**

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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? **Improve care for patients who qualify for treatment.** Would NHS staff need extra education and training? **Not specifically but would need to follow the protocols already available from Roche. We intend to publish a management algorithm for the treatment of skin toxicities which we hope to be available for users of the drug shortly after licensing.** Would any additional resources be required (for example, facilities or equipment)? **No additional resources required that are not already available in most secondary care settings**
Implementation issues