Appendix G - professional organisation submission template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Nivolumab for treating advanced (unresectable or metastatic) melanoma

Thank you for agreeing to make a submission 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 submission, 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, on behalf of the British Association of Dermatologists' Therapy & Guidelines and Skin Cancer sub-committees

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? ✓
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? ✓
- 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)?
- 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? **Depends on BRAF status and extent of disease when metastatic. Current available treatments are BRAF inhibitors, ipilimumab, pembrolizumab and standard chemotherapy (dacarbazine).**

Is there significant geographical variation in current practice? **Variation occurs dependent where trials are available.**

Are there differences of opinion between professionals as to what current practice should be? **Generally no but sequencing of treatment can vary.**

What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages? **BRAF inhibitors, ipilimumab, pembrolizumab and standard chemotherapy (dacarbazine). BRAF inhibitors can only be given in approx. 50% of patients with a metastatic melanoma who have a BRAF mutation. Ipilimumab can be used for all types of metastatic melanoma but does have significant autoimmune side effects so patients need to be fit. Pembrolizumab is also available for both BRAF positive and negative patients any line.**

Nivolumab plus ipilimumab is more effective than either ipilimumab on its own or nivolumab on its own as per the checkmate 067 trial (Larkin et al, NEJM).

Downsides of the combined treatment include that the toxicity is higher. The data however are not mature and so it is difficult to predict the longer term overall survival. There appears to be however no difference between BRAF positive or negative status. There is no direct comparison to the BRAF inhibitors.

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? **NO**

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? **Secondary care oncology clinics**

Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)? **Day care facilities need to be available as the drug is administered intravenously.**

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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. **There are new NICE melanoma guidelines but they were produced prior to this technology becoming available.**

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? **Requires intravenous administration fortnightly until progression of disease. Ipilimumab is a cycle of 4 IV treatments (usually) and the BRAF inhibitors are orally administered.**

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. **Stop on progression of disease and at present the data on how long it should be carried on for in disease responders is not known in view of toxicity.**

With immunotherapies; particularly ipilimumab, some early CT scans can show differential increase in the size of the disease which is secondary to the immune reaction rather than true progression. Interpretation of these scans can therefore be difficult and review at an MDT with specialist radiologist input is recommended.

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? **Autoimmune side effects are the most reported AE's but not as severe generally as ipilimumab.**

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.

Implementation issues

The NHS is required by the Department of Health 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 to vary this direction.

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

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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)?

Equality

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 this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/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 lead to recommendations that 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.