Professional organisation statement template

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 Maria Michelagnoli

Name of your organisation UCLH NHS Foundation Trust

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)?
- 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)

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.

Osteosarcoma is treated within sarcoma (or paediatric oncology) multi-disciplinary teams (MDTs) and involves multi-agent chemotherapy – neoadjuvant and adjuvant and surgery when possible. Due to the rarity of the disease, management of these cases is priotised via the MDTs and therefore there is minimal variation in practice nationally. Current practice for localised osteosarcoma uses a 3 drug regimen including cisplatin, doxorubicin and methotrexate. The role of ifosfamide (+etoposide) and interferon is being explored within the context of the current clinical trial – EURAMOS1.

Presentation with metastatic disease or recurrent disease, probably has a more divergent practice – but common agents would include cisplatin, doxorubicin, methotrexate, ifosfamide and etoposide.

The proposed role of mifurmatide would be additive post – operatively where complete resection had been obtained.

The alternatives to the proposed technology would include the role of ifosfamide and the place of biologic therapies eg interferon, dendritic vaccines, IGFR1 inhibition. Current practice is considering these options within clinical trial formats only. No improvements in disease free survival or overall survival have been observed in the UK over at least the last 1 -2 decades.

The role of mifurmatide in poor prognositc groups such as metastatic disease and relapsed disease has yet to be proven – clearly these are groups that require urgent research opportunities.

According to published data and one personal experience of the use of mifurmatide – I am not aware of sub-groups who would be disadvantaged by access to the technology.

I would perceive that mifurmatide aught to be utililised in the specialist setting only initially. With national experience of the technology a case at a later date may be made for accessing the product closer to home, once the patient was stabilised. (eg after standard chemotherapy had finished?). The patient would need access to specialist nursing – 1: initial experiences may be associated with significant fever and chills 2: the twice weekly treatment in the first 12 weeks coincides with the delivery of complex multi-agent chemotherapy programmes.

To my knowledge there has been very limited access to the technology in the UK to date. My own personal experience was via the compassionate access programme run previously by IDM, after the EMEA approval.

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?

From my own very limited practice the technology will initially require some skill to administer in practice. The current chemotherapy programme is already complex, time consuming and fraught with adverse events. Scheduling twice weekly infusions within this complex care setting will be challenging.

The initial doses may incur significant fever, chills and hypotension – hence the need to deliver in a specialist setting. Patient acceptibility of this scenario may limit compliance. My limited experience of managing these side effects are that the symptoms can be safely managed with clear protocols – using anti-pyretics and hydrocortisone.

The protocols for usage of the product would need to include clear management guidelines of these side effects. The reported experience is that these side effects reduce over time/exposures.

However the practice on which the RCT was conducted is broadly similar to UK practice currently and therefore I feel it is appropriate to extrapolate the trial findings to NHS practice.

The most important outcome is the evidence that this technology appears to offer a significant improvement in chances of survival in a patient group with an ultra-orphan disease, which has seen a plateauing of improvement over the past 2 decades despite other imrpovements in cancer/supportive care. The concern is the hope that other patients with osteosarcoma with poorer prognoses eg presentation with metastatic or relapsed disease may also have a chance of access to this product – as meaningful RCTs in an appropriate time context are unlikely.

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.

I am not privy to other evidence

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 ideal situation would be a uniform roll-out access to the product via the sarcoma MDTs. The complies with equitable access for patients in this very rare situation.

Clear guidelines for use of the technology could be accessed via the sarcoma MDTs.