Clinical Expert Statement Template

Thank you for agreeing to give us a personal statement on your 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. Your statement can be as brief as you like, but we suggest a maximum of 8 pages.

If there are special reasons for exceeding this 8-page limit please attach an Executive Summary to your statement.

What is the place of the technology in current practice?

*As a paediatrician the scope of my responses has been specifically targeted to cover the use of these technologies in children.

How is the condition currently treated in the NHS?

Amantadine is not (widely) used. Zanamivir and Oseltamivir are recommended for use in high-risk adults or children >12 years. Oseltamivir is recommended for treatment of high-risk children presenting with influenza symptoms of less than 48 hours duration during influenza A or B outbreaks.

For the purposes of the paediatric age range high risk is defined as:

1. A diagnosis of asthma. 2. A diagnosis of any other chronic respiratory disease. 3. Immunodefieciency. 4. Diabetes mellitus. 5. Significant cardiovascular disease ie cyanotic congenital heart disease or any degree of heart failure. 6. Chronic renal disease.

Is there significant geographical variation in current practice?

None that I am aware of. However, data on compliance with influenza vaccination in asthmatic children suggests a significant practice-to-practice variation. This has been attributed to physician ambivalence.

Are there differences in 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?

Oseltamivir is not widely used in the hospital setting in children in the UK.

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?

The data available to me doesn't really suggest a big difference in benefit to 'at-risk' children as the data is variously 'out-of-date' (Neuzil KM et al. NEJM 2000;342(4):225-231) or flawed/multiple analyses have been undertaken (O'Brien et al Pediatrics 2004;113:585-593.).

Nonetheless there is some data suggesting a reduction in exacerbation rates and improvement in lung function in children with asthma treated with oseltamivir. (Johnston SL et al. Ped Inf Dis J 2005;24(3):225-232.). However, the primary end point for the study (freedom from illness) was not met.

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)?

Osletamivir could be potentially used in primary or secondary care.

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?

With regard to the paediatric population oseltamivir is licensed for use in children over the age of 1. The group with the highest incidence of complications and hospitalisations is children under 1 year. I am not aware of unlicensed use.

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.

None known (although previous NICE guidance 2003).

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology in clinical practice reflects that observed under clinical trial conditions. 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?

I think this is reflected in my answers above. The evidence base in children is limited. Nonethless, it appears highly likely that oseltamivir is helpful in reducing the incidence of chest infections (pneumonia) and otitis media. The latter is unlikely to be a major burden to health care systems. The former is potentially important in reducing morbidity, hospital use and mortality.

Clinical experience from secondary care suggests that increasing numbers of families are choosing to access urgent healthcare via Children's Emergency Services in secondary care. We are seeing increasing numbers of children early in the course of diseases and therefore we may have increasing scope to prescribe oseltamivir.

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 outcomes from trials include duration of illness, health care utilisation and estimated overall health care costs. Each has merit although harder outcomes such as ventilation episodes and/or death rates would be welcome. These would require a massive study.

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?

Side effects seem to be limited although there is a widely-reported increase in nausea. This would be difficult to ascertain in younger children.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, if already available, compares with current alternatives used in the UK.
Is the technology 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 use?

Oseltamivir seems relatively easy to use (oral preparation, well-tolerated). In intention to treat analyses >90% of children manage to stick to the protocol within the confines of a clinical trial. Clearly zanamivir (diskhaler) would not be suitable for younger children and given the concerns about potential bronchospasm seems an unlikely 'first choice' in the paediatric population. It is likely to be acceptable to parents. Nonetheless there is some evidence of improved efficacy against Influenza B (Kawai N et al. 2008 J Infect 56:51-7.) In a predominantly Influenza B year this might have to be taken into consideration.

I would echo concerns raised during the initial review of these technologies in 2003. Namely, that use of this technology may increase overall attendance at hospital with other viral illnesses during an influenza outbreak. Even small increases in demand during the winter periods place considerable burdens on resources and place all children seen within these services at increased risk. Given the rather non-specific nature of symptoms in infants we could justify prescription (and hence deliver the undesired message that attendance was necessary) of large amounts of oseltamivir.

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.

N/A.

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.

1. Discussion with colleagues and hospital pharmacy at Derbyshire Children's Hospital. Oseltamivir not used at all in last 12 months.

Implementation issues

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)?

Please note: The NHS is required by the Department of Health and 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 Welsh Assembly Government to vary this direction.
Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

Oseltamivir could be widely prescribed and administered without substantial changes in staff training. The cost would place a burden on the health care community that would at least be partially offset by a decrease in health care utilization overall (current estimates are that these benefits are likely to be marginal). The prescription costs for children seen in the Children's A&E setting would be higher than the tariff rate for seeing them and would put considerable burden on the prescribing budgets of hospitals.

In truth these could only be funded by cost improvements elsewhere.