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:

[redacted]

Name of your organisation

Representing British Society for Gastroenterology

Are you (tick all that apply):

- I am a specialist in the treatment of people with the condition for which NICE is considering this technology?

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

Entecavir is:

- more potent than lamivudine, adefovir and telbivudine; more patients achieve HBV DNA negativity at 6mths and there is a more rapid decline in HBV DNA;
- significantly less likely to give resistance at 1, 2, and 3 years after starting treatment;
- is cheaper, in our hospital, than using a combination of lamivudine and adefovir.

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice?

At [redacted] we have followed the current NICE guidelines which recommend for HBe antigen positive and negative cases that we offer a trial of pegylated interferon for up to 12 months and in those that fail to achieve a sustained response, we offer the following:

For those with HBV DNA > or = 10^7copies/ml:
either combined lamivudine 100mg and adefovir 10mg/day
or entecavir 0.5mg.

For those with HBV DNA < 10^7copies/ml:
Lamivudine 100mg and for those with an incomplete response (remaining detectable HBV DNA at 6 months) addition of adefovir 10mg.

Are there differences of opinion between professionals as to what current practice should be?

Some physicians will:
- not offer pegylated interferon, preferring to start with nucleos/tide therapy;
- give combination therapy to all viraemic patients from the start.

What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

There are two families of nucleos/tide analogues exhibiting cross resistance within each family but not between families.

Family 1 includes
- lamivudine (L);
- emtricitabine (available with tenofovir as truvada) (NL)
- telbivudine (L);
- entecavir (L).

Family 2 B includes:
- adefovir (L)
- tenofovir (NL).
- :

Entecavir is:
- more potent than lamivudine, adefovir and telbivudine, more patients achieving HBV DNA negativity at 6mths and a more rapid decline in HBV DNA;
- significantly less likely to give resistance at 1, 2, and 3 years after starting treatment;
- is cheaper than using a combination of lamivudine and adefovir.

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 cirrhosis should not be given interferon but should start on the most potent nucleos/tide analogue with the lowest risk of developing drug resistance: at the moment this is entecavir.

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)?

Because of the danger of drug resistance, treatment is supervised from hospital Hepatology/GI Units.

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?

Because of cost the uptake around the country is variable.

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.

Best Practise in Rx of CHB: a summary of the European Viral Hepatitis Educational Initiative (EVHEI)
J Hepatology 2007 October 47 588-597.

The advantages and disadvantages of the technology

Entecavir has the advantage of having low resistance rates comparable to those seen with combination treatment with lam and adefovir. Although experience is limited to 3 years of therapy there have been few if any significant side effects. It should be born in mind however that therapy will need to continue for many years in most cases (Nowak et al 1996 PNAS 93 4398).
Resistance occurs more frequently if patients have had prior therapy with lamivudine; entecavir should therefore probably be used as first line therapy.

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.

In our hospital entecavir is the drug of first choice in those with high HBV DNA levels (10^7 or greater).

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?

The trials were conducted under conditions that allow extrapolation to UK patients with evidence of progressive disease (stage 1 or more fibrosis).

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 endpoint is rapid control of HBV replication as indicated by HBV DNA being undetectable by sensitive PCR.

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?

A tumour was found in rats but there has been no suggestion of similar problems in humans

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.

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)?

This therapy is likely to add substantially to the cost of care of those with HBV liver diasease but Liaw et al (NEJM 2004 351 1521), using lamivudine , have shown that these anti-viral therapies significantly prolong life and are cost effective.
The therapy can be delivered, alongside therapy for HCV induced liver disease, in the developing Hepatology Networks. It is estimated that between 180,000 and 325,000 cases exist and around 30% of these will die of cirrhosis or HCC if untreated. These cases occur in ethnic minority groups.
Some patients will not require treatment if HBV DNA is undetectable or $<10^4$