NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

SCOPE

Clinical guideline title: Hepatitis B (chronic): diagnosis and management of chronic hepatitis B in children, young people and adults.

Quality standard title: Hepatitis B (chronic)

1 Introduction

1.1 Clinical guidelines

Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions within the NHS. They are based on the best available evidence.

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

1.2 Quality standards

Quality standards are a set of specific, concise quality statements and measures that act as markers of high-quality, cost-effective patient care, covering the treatment and prevention of different diseases and conditions.

For this topic a NICE quality standard will be produced based on the guideline recommendations. The clinical guideline and the quality standard will be published at the same time.

This scope defines the areas of care for which specific quality statements and measures will (and will not) be developed.

The guideline and quality standard development processes are described in detail on the NICE website (see section 8).

2 Need for guidance

2.1 Epidemiology

a) Chronic hepatitis B is defined as hepatitis B infection that continues for longer than 6 months. It is a major healthcare problem in the UK. The estimated prevalence of chronic hepatitis B in the UK is 0.3% (so approximately 180,000 people have the condition). The prevalence considerably higher among high-risk groups such as first generation migrants from areas where hepatitis B is endemic, people who have multiple sexual partners, and injecting drug users is. The number of notifications of hepatitis B to the Health Protection Agency has risen sharply, from 435 cases in 1990 to 1151 in 2003.

b) Currently, there are approximately 600 to 800 new cases of symptomatic (jaundiced) acute hepatitis B infection each year. In 50% of cases there is no obvious risk factor, 20% of cases relate to intravenous drug use, and 25% are sexually acquired (80% of these in men who have sex with men). In most cases the infection is thought to come from people with chronic hepatitis B who are asymptomatic.

c) The risk of chronic infection is closely related to age at acquisition and varies from 5% in adulthood to more than 90% in perinatal infection.

d) Chronic hepatitis B most commonly follows childhood infection, and thus people often present to health services after many years of asymptomatic infection (often unknown to the patient).

e) Treatment is indicated for those at highest risk of progressive of liver disease and its complications, and aims to reduce viral loads.

Multiple studies have shown that therapeutic reduction in viral loads leads to a marked reduction in fibrosis progression and risk of cirrhosis. Among people who already have cirrhosis the risk of liver complications, including hepatocellular carcinoma, is also reduced.

f) Long term studies of the clinical outcome for the most recently approved nucleoside or nucleotide analogue treatments are not yet available, but early studies (which have been running for up to 5 years) show these have the most potent effect on viral loads and liver histology, and are likely to have the greatest impact on complications.

2.2 Current practice

a) The diagnosis of chronic hepatitis B infection includes the use of immunoassays for hepatitis B surface antigen (HBsAg), hepatitis B 'e' antigen (HBeAg; people with hepatitis B may be either HBeAg positive or negative) and antibodies to hepatitis B surface antigen (HBeAb), and quantitative hepatitis B virus DNA assay. Co-infections with hepatitis C, hepatitis D and HIV are also identified by serological assay.

b) To assess the phase of chronic hepatitis B, routine liver function tests are performed and serological assays are used to detect hepatitis B virus antigens (HBeAg) and antibodies (the antibody to hepatitis B 'e' antigen, known as HBeAb).

c) Two classes of drug are currently used in treating chronic hepatitis B: pegylated interferon and nucleoside or nucleotide analogues. Four nucleoside or nucleotide analogues are currently recommended by NICE and are in widespread clinical use.

d) Pegylated interferon suppresses the virus in a smaller proportion of patients than nucleoside or nucleotide analogues (especially entecavir and tenofovir) but is given for a fixed duration (24 or 48

weeks), whereas nucleoside or nucleotide analogues often need to be used as long term treatment.

e) If needed, nucleoside or nucleotide analogue therapy may be given after pegylated interferon. A single large trial did not show combination therapy with both pegylated interferon and lamivudine to be advantageous.

f) Combination nucleoside or nucleotide analogue treatment may be necessary to reduce the risk of or treat established resistance.

g) The earliest licensed nucleoside or nucleotide analogues (lamivudine and adefovir) are less effective than the more recently approved agents (entecavir and tenofovir), judged according to the proportion of patients achieving undetectable viral loads, seroconversion rates and rates of resistance.

h) Telbivudine is licensed for treating hepatitis B but is not recommended by NICE because of high drug resistance rates.

i) Tenofovir in combination with emtricitabine is used in people with chronic hepatitis B, but is only licensed at present for HIV infection.

j) NICE technology appraisal guidance 96, ' Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B' compares interferon, lamivudine, and adefovir, but otherwise NICE guidance considers each drug for hepatitis separately. Cross resistance may occur between agents so pre-treatment with lamivudine increases the chance of viral resistance to entecavir.

k) Patient information and counselling provided to family members by healthcare professionals should include treatment options, risk of other family members being infected and the benefits of vaccination.

l) Several audits have shown significant variation in practice. For example, a recent audit in London showed that only two thirds of people with chronic hepatitis B diagnosed in primary care were referred for assessment. There is also strong anecdotal evidence of wide variation in prescribing practice with regard to initial choice of agents and duration of therapy, particularly after HBe antigen/anti-HBe seroconversion. This guideline is needed to reduce variation and improve the care of people with chronic hepatitis B.

3 Clinical guideline

3.1 Population

3.1.1 Groups that will be covered

a) Children, young people and adults with chronic hepatitis B including:

- people co-infected with HIV, hepatitis C or hepatitis delta (D) virus
- Immunocompromised people (such as those undergoing cancer treatments) who are carriers or have been previously infected, for whom prophylactic treatment might be beneficial
- pregnant and lactating women
- people with cirrhosis, including those with liver decompensation.

3.1.2 Groups that will not be covered

a) People who have had a liver transplant.

b) People with acute hepatitis B.

3.2 Healthcare settings

a) Primary, secondary, tertiary and community NHS settings.

3.3 Diagnosis and management

3.3.1 Key issues that will be covered

Identification and assessment of chronic hepatitis B

a) Setting of initial tests (for example, primary or secondary care).

b) Criteria for referral to specialist services.

c) Laboratory tests to determine severity of fibrosis and whether treatment needs to be started:

- liver biopsy
- non invasive methods of assessing liver fibrosis (for example, serum fibrosis markers, elastography, aspartate aminotransferase/platelet ratio index [APRI]).

d) Diagnosis of concomitant infections.

Pharmacological treatment

e) Sequential and combination drug therapy for specified subgroups:

- adefovir
- emtricitabine
- entecavir
- lamivudine
- pegylated alpha-interferon
- telbivudine
- tenofovir.

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Monitoring stages of condition

f) Surveillance timing, and frequency of:

- quantitative DNA assays and resistance genotyping
- case finding for hepatocellular carcinoma
- adverse events, in particular renal toxicity
- stopping points for treatment according to HBeAg status.

g) Patient information.

3.3.2 Key issues that will not be covered

a) Primary prevention of hepatitis B, including vaccinations and case finding.

b) Signs and symptoms of hepatitis B.

c) Access issues related to case finding.

d) Non-pharmacological management of chronic hepatitis B.

e) Co-infection of chronic hepatitis B with hepatitis viruses A or E.

f) Guidance on working practices for infected healthcare workers.

g) Liver transplantation.

h) Acute hepatitis B.

3.4 Main outcomes

a) Disappearance of serum hepatitis B DNA, tested by the most sensitive available quantitative assay (12 IU/ml)).

b) Regression of fibrosis stage.

c) Clearance of HBeAg and HBsAg.

d) Frequency of liver decompensation and incidence of hepatocellular carcinoma.

e) Improved quality of life, tested using a validated general instrument or a validated liver disease-specific instrument.

f) Mortality.

g) Adverse effects.

3.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see section 8).

4 Quality standard

Information on the NICE quality standards development process is available on the NICE website, see section 8.

4.1 Mapped areas of care

The areas of care in a patient's journey that will inform the development of the quality statements are set out in section 5.

4.1.1 Areas of care from the guideline that will be considered

a) The setting for initial tests to identify chronic hepatitis B and referral to specialist services.

b) Assessment of hepatitis B in secondary care

c) Information for patients.

d) Pharmacological treatment for management of chronic hepatitis B including sequential and combination therapies for specific populations.

e) Monitoring of stage of chronic hepatitis B including timing and frequency of tests.

4.1.2 Areas of care that will be considered using other NICE guidance

None

4.1.3 Areas of care that will not be considered

a) Primary prevention of hepatitis B including vaccinations and case finding.

b) Signs and symptoms of hepatitis B.

c) Access issues related to case finding.

d) Non-pharmacological management of chronic hepatitis B.

e) Co-infection of chronic hepatitis B with hepatitis viruses A or E.

f) Guidance on working practices for infected healthcare workers.

g) Liver transplantation.

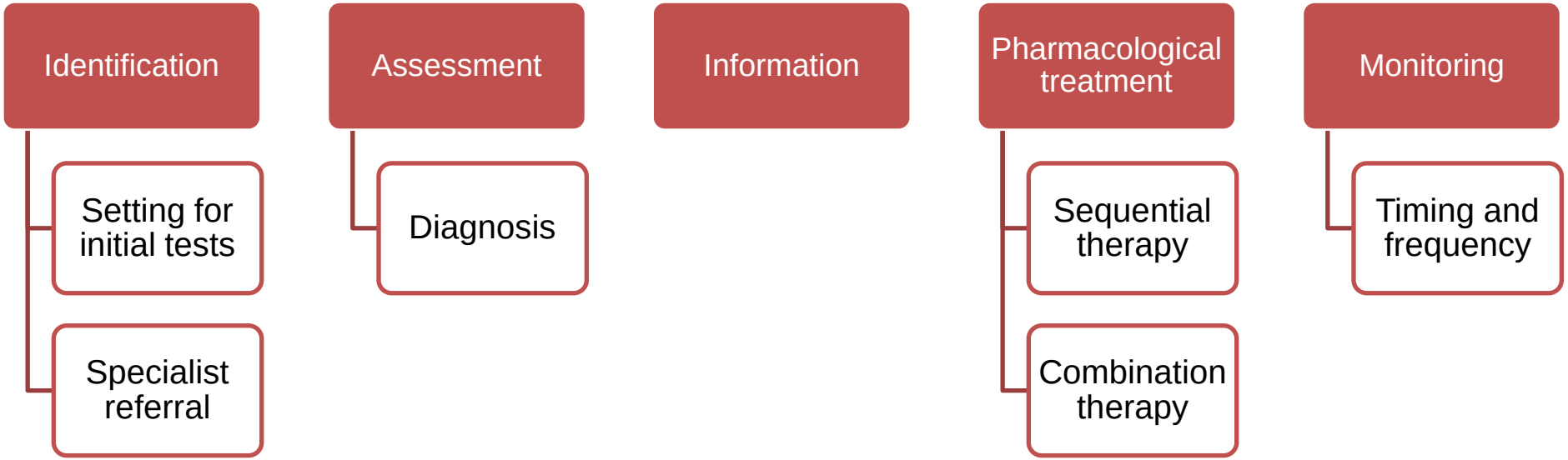
h) Acute hepatitis B.

4.2 Economic aspects

Developers will take into account both clinical and cost effectiveness when prioritising the quality statements to be included in the quality standard. The economic evidence will be considered, and the cost and commissioning impact of implementing the quality standard will be assessed.

5 Mapped areas of care

The diagram below sets out the areas of care that NICE will consider covering in the quality standard. The content of the final quality standard may differ after consultation with stakeholders.



6 Status

6.1 Scope

This is the consultation draft of the scope. The consultation dates are 14 June 2011 to 5 July 2011.

6.2 Timings

The development of the guideline recommendations and the quality standard will begin in September 2011.

7 Related NICE guidance

7.1.1 NICE guidance that will be incorporated in or updated by the clinical guideline

This guideline will incorporate[1] the following NICE guidance:

- Tenofovir disoproxil fumarate for the treatment of hepatitis B. NICE technology appraisal guidance 173 (2009). Available from www.nice.org.uk/guidance/TA173
- Telbivudine for the treatment of chronic hepatitis B. NICE technology appraisal guidance 154 (2008). Available from www.nice.org.uk/guidance/TA154
- Entecavir for the treatment of chronic hepatitis B. NICE technology appraisal guidance 153 (2008). Available from www.nice.org.uk/guidance/TA153
- Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B. NICE technology appraisal guidance 96 (2006). Available from www.nice.org.uk/guidance/TA96

[1] subject to the outcome of the Technology Appraisal review proposal consultation with consultees

7.2 Related NICE guidance

Published

- Medicines adherence. NICE clinical guideline 76 (2009). Available from www.nice.org.uk/guidance/CG76
- Obesity. NICE clinical guideline 43 (2006). Available from www.nice.org.uk/guidance/CG43
- Alcohol dependence and harmful alcohol use. NICE clinical guideline 115 (2011). Available from www.nice.org.uk/guidance/CG115
- Increasing the uptake of HIV testing among men who have sex with men. NICE Public health guidance 34 (2011) Available from: www.nice.org.uk/guidance/PH34
- Increasing the uptake of HIV testing among black Africans in England. NICE Public health guidance 33 (2011). Available from: www.nice.org.uk/guidance/PH33

NICE guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Patient experience in generic terms. NICE clinical guideline. Publication expected October 2011.
- Hepatitis B and C: ways to promote and offer testing. NICE public health guidance. Publication expected December 2012.

8 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual
- 'Developing NICE quality standards: interim process guide'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual and

www.nice.org.uk/aboutnice/qualitystandards). Information on the progress of the guideline and quality standards is also available from the NICE website (www.nice.org.uk).