**National Institute for Health and Clinical Excellence**

# Hepatitis B – Clinical Guideline and Quality Standard
# Scope Consultation Table
# 14.06.2011 – 05.07.2011

| Type | Stakeholder | Order No | Section No | Comments<br>Please insert each new comment in a new row. | Developer's Response<br>Please respond to each comment |
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| SH | Abbott Diagnostics | 1.0 | 3.3.1.f | As well as use of DNA tests here you should consider use of quantitative HBsAg by serology as it is cheaper than DNA testing | Thank you for your suggestion, this has been noted and the scope has been amended to reflect this. |
| SH | British Association of sexual health and HIV (BASHH) | 1.01 | 3.3.1 | We are pleased that the diagnosis of concomitant infections such as HIV will be considered in this guideline. The treatment of Hepatitis B monoinfection will differ from co-infection with HIV as regimens such as tenofovir monotherapy cannot be used as it would compromise the treatment of HIV infection. We would welcome a clear sections on issues pertaining to HIV co-infection such as diagnosis, referral criteria, when to start hep B treatment and what with. | Thank you for your comment.This was not an area prioritised for inclusion following the scoping exercise. There is guidance already available on Hepatitis B in people co-infected with HIV produced by the British Association for Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA). |
| SH | RCGP | 3.0 | General | The scope seems appropriate however the reference to diversity and equality is implied rather than stated | Thank you for your comment. We have chosen to state that we will include all people with chronic Hepatitis B except those specified in the groups that will not be covered in this section, rather than list all subgroups such as migrant and other high risk populations. We are aware of equality issues for some subgroups and this will be addressed by the GDG when reviewing the evidence. |
| SH | RCOG | 3.1 | General | Pleased that pregnant and lactating women are to be included. Assume that antenatally diagnosed infection is included since it does not appear to be specifically excluded; this is an important area. | Thank you for your comment. This issue will be covered in the guideline. |

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| SH | RCOG | 3.2 | 3.3.1 | Pharmacological treatments unlikely to be licensed for use during pregnancy and lactation but encourage you to provide advice regardless of this. | Thank you for your comment. |
| SH | RCOG | 3.3 | 3.3.2 | Primary prevention is not covered; assuming that vertical transmission from mother to infant is considered primary, ask that this be considered since it is important and highly relevant. | Thank you for your comment. We agree that this issue is important but is established practice and covered in 'Immunisation against infectious disease (The Green Book) - 2006 updated edition'. |
| SH | RCOG | 3.4 | 3.4 | Main outcomes. Wish to see rates of vertical transmission (mother to infant) as an outcome measure. | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |
| SH | British Liver Trust | 4.0 | 2.2.k | The British Liver Trust produces a range of publications that should be included in the scope. These are lay and professionally reviewed, and are available from our website in pdf form if you wish them to be included. Expansion on the patient information topic to specify what information is provided by clinicians is key to successful treatment of patients. | Thank you for your comment. We note the publications available from the British Liver Trust. The topics to be covered within the patient information section of the guideline will be agreed with the Guideline Development Group. Thank you for your suggestion. |
| SH | British Liver Trust | 4.1 | 3.3.2 a | Not including 'vaccinations and onward transmission' will be at odds with the patient information section that will be included in the scope. As this is a transmissible disease, we feel that information about vaccination and familial onward transmission should be included in this discussion to ensure that patients are fully informed of the risks surrounding Hep B. | Thank you for your comment. This area is included in section 4.2.1 (a) and (e) of the scope of the NICE Public Health guidance for Hepatitis B and C which is due to be published in December 2012. Vaccination is also covered by 'Immunisations against infectious disease (The Green Book) - 2006 updated edition'. NICE has also made a recommendation on Neonatal Hepatitis B in its guidance on reducing differences in the uptake of immunisations. |
| SH | British Liver Trust | 4.2 | 4.1.1 c | Information for patients should include others at risk, how the disease is transmitted, and keeping safe. | Thank you for your comment, this has been noted. Aspects of this are also covered in the scope of the |

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| | | | | Access to patient and carer support should also be considered within this topic. The provision and dissemination of information surrounding patient support will fall within the patient information topic. | NICE Public Health guidance for Hepatitis B and C which is due to be published in December 2012. |
| SH | BSPGHAN | 5.0 | | **No comments** | Thank you. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.1 | General | Comment: The HPA's BBIPB Strongly support the development of the guidelines; HPA standards for local surveillance and follow up are relevant and available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947376936 and should be reviewed once the guidelines are published. HPA staff will have a role in encouraging patient referral for treatment and vaccination for household/sexual contacts. | Thank you for your comment. We will take this into consideration during guideline development. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.2 | 2.1 (a) | Suggest the following text to solve comment No's 3, 4 and 6:<br>"Hepatitis B virus (HBV) infects humans and causes both an acute and a chronic infection. Chronic hepatitis B infection (chronic HBV) is generally defined bythe persistence of hepatitis B surface antigen (HBsAg) in the plasma of a patient that continues for longer than 6 months. The disease that this may cause is called chronic hepatitis B and is a major healthcare problem in the UK. The estimated prevalence of chronic HBV 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 HBV is of high endemicity. Acute hepatitis B is seen more commonly in people whose sexual partners are chronically infected by HBV, people who have multiple sexual partners and injecting drug | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |

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| | | | | users. The incidence of acute hepatitis B is monitored and the number of notifications of acute hepatitis B to the Health Protection Agency has risen sharply, from 435 cases in 1990 to 1151 in 2003." | |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.3 | 2.1 (a) | "Chronic hepatitis B is defined as hepatitis B infection that continues for longer than 6 months."<br><br>Comment: There is a problem with this definition as once infected many people, even after clearance, remain infected (even if this is occult). They probably only declare this once they become immunosuppressed. Chronic hepatitis B is by definition liver disease caused by persistent hepatitis B virus infection. | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.4 | 2.1 (a) | "The estimated prevalence of chronic hepatitis B in the UK is 0.3%"<br><br>Comment: The prevalence figures relate to chronic Hepatitis B Virus (HBV) and NOT to chronic hepatitis B. Please see suggested text at comment 4. | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.5 | 2.1 (a) | "from areas where hepatitis B is endemic,"<br><br>Comment: The UK could be considered endemic but low prevalence. Please see suggested text at comment 4. | Thank you for your suggestion. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.6 | 2.1 (a) | The incidence of hepatitis B has risen sharply, from 435 cases in 1990 to 1151 in 2003."<br><br>Comment: This is incidence, not prevalence. See suggested text at comment no. 4. | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.7 | 2.1 (c) | Suggest the following replacement text:<br>"c) The risk of *the acute infection progressing to a* chronic infection is closely related to age at acquisition and varies from 5% in adulthood to more | Thank you for your suggestion. This has been noted and the scope has been amended to reflect this. |

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| | | | | than 90% in perinatal infection." | |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.8 | 2.2 (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)"<br><br>Comment: Essentially patients may have HBeAg positive or anti-HBe positive. HBeAg negative is usually a transit time from HBeAg positive to anti-e positive) | Thank you for your comment. This change has been made. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.9 | 2.2 (a) | Suggest following replacement text<br>"antibodies to hepatitis B surface antigen (HBsAb), and *molecular assays* for hepatitis B virus DNA."<br><br>Comment: Text changed to reflect use of both quantitative and qualitative assays. | Thank you for your suggestion. However we do not think a change is required. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.10 | 2.2 (a) | Suggest following replacement text:<br>"To assess the phase of chronic hepatitis B, routine liver function tests are performed, serological assays are used to detect hepatitis B virus *e*-antigen (HBeAg) and antibodies (the antibody to hepatitis B 'e' antigen, known as *anti-HBe*) *and molecular assays to measure HBV DNA are undertaken*." | Thank you for your suggestion. This has been noted and the scope has been amended to reflect this. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.11 | 2.2 (d) | Comment: Please check use of interferon. | Thank you for your comment. The scope has been amended. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.12 | 2.2 (f) | "Combination nucleoside or nucleotide analogue treatment may be necessary to reduce the risk of or treat established resistance"<br><br>Comment: Please define what you mean, known genotypic resistance or clinical resistance. | Thank you for your comment. We are referring to any type of resistance. |
| SH | HPA Borne Infections Programme Board (BBIPB) | 5.13 | 2.2(k) | Comment: We would like to see sexual partners included here e.g. family members/sexual partners… | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |

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| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.14 | 3.1.1 (a) | Comment: We are pleased that pregnant women are included and would like specific mention in the guideline of the importance of follow up of babies born to hepatitis B positive mothers and roles of maternity units and primary care or at the least a link to national best practice/care pathway: http://www.dh.gov.uk/en/Publichealth/Immunisation/Keyvaccineinformation/DH_125275 | Thank you for your suggestion. Both pregnant and lactating women are included in the scope and management of babies will be addressed by the guidance. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.15 | 3.1.1 (a) | Suggest following replacement text:<br>Children, young people and adults with chronic hepatitis B *virus infection* including:<br><br>Comment: It is better to refer to chronic HBV infection so that all carriers are assessed and not just those with disease. | Thank you for your comment. This has been addressed and the scope has been amended. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.16 | 3.1.2 (a) | "People who have had a liver transplant"<br><br>Comment: Please justify why not included. | Thank you for your comment.<br>People who had a liver transplant are excluded because it is a very small group due to highly effective preventative treatment. According to the British Liver Trust there were only 663 liver transplants in the UK and the three most common causes were alcohol abuse, hepatitis C and primary biliary cirrhosis (not associated with hepatitis B). Because of this, we did not feel this area was a high priority to consider given the time and resource available. |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.17 | 3.1.1 (b) | "People with acute hepatitis B."<br><br>Comment: There is a move to treat early acute | Thank you for your comment. This is outside the remit of the guideline. |

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| | | | | infection with nucleos/tides, why not mention this is being examined. Certainly if identified an early infection, i.e. DNA/HBsAg seropositive without anti-HBc could be referred to a hepatologists for treatment. | |
| SH | HPA Blood Borne Infections Programme Board (BBIPB) | 5.18 | 3.4 (c) | Suggest following text:<br><br>Clearance of HBeAg and seroconversion for anti-HBe<br><br>Clearnace of HBsAg and seroconversion for anti-HBs<br><br>Comment: These two are not concomitant. | Thank you for your suggestion, this has been noted and the scope has been amended to reflect this. |
| SH | UK National Screening Committee | 6.0 | 3.1.1 Groups that will be covered<br><br>a) Children, young people and adults with chronic hepatitis B including:<br><br>& | There may be an inconsistency between the two highlighted paragraphs.<br><br>3.1.1 states that the population to be covered by the guideline will be those with chronic hepatitis B whereas 3.3.1 suggests that the tests, processes through, and settings in, which chronic infection is identified will be covered.<br><br>The second may overlap with the UK NSC's remit and could be clarified.<br><br>One option might be to start 3.3.1 with the current 'b) criteria for referral to specialist services'.<br><br>This would be consistent with the aim of the guideline which is to improve the care of people with chronic HBV by reducing variation in referral to specialist services and in prescribing practice. | Thank you for your comment. This has been noted and the scope has been amended to reflect that we are not including initial diagnosis but looking at the setting of pre-therapeutic tests. |

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| | | | 3.3.1 Key issues that will be covered<br><br>Identification and assessment of chronic hepatitis B<br><br>a) Setting of initial tests (for example, primary or secondary care). | If it is necessary to include a discussion of the settings in which 'initial tests' take place this should be consistent with the UK NSC's recommendations in this area.<br><br>This applies equally to the quality standard 4.1.1 | |
| SH | UK National Screening Committee | 6.1 | 3.1.1 Groups that will be | It is very positive that management of pregnant women will be included in the guidance. The criteria for referral to specialist services should be consistent with the standards issued by the | Thank you for your comment. We will take this into consideration during the guideline development. |

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| | | | covered<br><br>Pregnant women | Infectious Diseases in Pregnancy Screening Programme in 2010. | |
| SH | UK National Screening Committee | 6.2 | 3.3.2 Key issues that will not be covered<br><br>h) acute hepatitis B | While acute hepatitis B is not included in the guideline there is a discussion of it (eg numbers of new cases / year at 2.1 b)) in the introduction which may not be necessary. | Thank you for your comment. We have provided this in the introduction as additional background information. |
| SH | UK National Screening Committee | 6.3 | General | It isn't clear if the intention is to include the criteria for referral etc for babies born to hepatitis B positive women who are tested at 12 months and found to HBsAg positive.<br><br>This is the endpoint of a vaccination pathway, itself variably implemented, and the starting point of clinical management for that child. Some guidance for these instances may be useful. | Thank you for your comment. This issue will be included in the guideline |
| SH | UK National Screening Committee | 6.4 | | Vaccination might be considered part of the management of babies born to hepatitis B positive women rather than primary prevention. Although this area is well documented it may be useful to cross refer to other sources of guidance to ensure completeness. | Thank you for comment. This is noted and will be considered during guideline development. We will refer to 'Immunisation against infectious disease (The Green Book) - 2006 updated edition', where appropriate. |
| SH | British Association for Adoption and Fostering | 7.0 | general | This response is being submitted on behalf of the BAAF Health Group, which is also a special interest | Thank you for your comment. We will include evidence related to all children and If there is any |

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| | (BAAF) | | | group of the Royal College of Paediatrics and Child Health (RCPCH), in consultation with social care professionals. The Health Group was formed to support health professionals working with children in the care system, through training, the provision of practice guidance and lobbying to promote the health of these children. With over 500 members UK-wide, an elected Health Group Advisory Committee with representation from community paediatricians working as medical advisers for looked after children and adoption panels, specialist nurses for looked after children, psychologists and psychiatrists, the Health Group has considerable expertise and a wide sphere of influence.<br><br>Our area of concern is the particularly vulnerable group comprised of looked after and adopted children and young people. | evidence found for the group of looked after and adopted children, this will also be included in the guideline. |
| SH | British Association for Adoption and Fostering (BAAF) | 7.1 | general | The issue of engagement with services must also be addressed, and is a particularly problematic issue in working with looked after children and young people and their families. Agreement to undergo testing is only the first step, and innovative services for the most vulnerable may need to be developed so that results are explained and individuals successfully engage in treatment over the long term. | Thank you for your comment, We agree this is an important issue and this has been noted. |
| SH | British Association for Adoption and Fostering (BAAF) | 7.2 | 3.1.1.a. | While we appreciate that the guidelines will address children and young people, it would be useful to specify that the particularly vulnerable population of children who are looked after, including those with a plan for adoption, will be considered. These children not only come from backgrounds which put them at high risk for blood borne infections, but are doubly disadvantaged by lacking committed parental | Thank you for your comment. We recognise the particular issues of this group of children. We will be looking at diagnosis and management of all children and young people with chronic hepatitis B. |

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| | | | | advocacy for high quality health provision. Indeed, for many of them risk of exposure to Hepatitis B and C arises from birth mothers misusing substances during pregnancy (vertical transmission) and early childhood. Furthermore when they become looked after, all too often health and social care agencies which share corporate responsibility fail to identify their risk and offer appropriate interventions.<br><br>It is also well recognised that young people who are looked after engage in high risk behaviour including substance misuse and sexual activity which places them at high risk of horizontal transmission of hepatitis.<br><br>The scope and guidance should specifically identify and address this population of children and young people to improve awareness by the diverse professional groups who have the opportunity to engage with them, including general practitioners, sexual health clinics, drug and alcohol services, obstetricians, neonatologists, midwives, as well as medical advisers and specialist nurses for looked after children.<br><br>It would also be useful to specify that the population of adopted and looked after children also includes asylum seeking refugee children and children adopted from abroad, many of whom were born in countries where the viruses are endemic. | |
| SH | British Association for Adoption and Fostering (BAAF) | 7.3 | 3.2.a | Looked after children and young people tend to be seen by health professionals in a wide variety of settings, yet their high risk of blood borne infections is often poorly recognised, even within services | Thank you for your comment. The guideline will be contributing to addressing these issues by looking at the pre-specified areas of diagnosis and management of chronic hep B in children, including |

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| | | | | targeted at them. It is therefore essential that guidelines specifically flag their high risk status in all possible settings to raise awareness amongst all who might play a role in early diagnosis. There is a risk that the most vulnerable client group, described above, namely children born to at risk mothers who sometimes DESPITE mother's status being known, still slip through the net. Our medical adviser members regularly see children who have become looked after, who have missed out on neonatal testing and immunisation/treatment, despite their birth mothers' positive hepatitis status being known at delivery. | those who are looked after. |
| SH | Department of Health: National Liver Disease Strategy | 8.0 | 2.2b | In addition to staging infection, staging of liver disease informs treatment options. This should be considered here (Liver biopsy, fibrosis markers etc) as well as later | Thank you for your comment. This has been addressed and the scope has been amended. |
| SH | Department of Health: National Liver Disease Strategy | 8.1 | 3.1.1 | Immigrant populations, or at least people born in specified other countries ought to form part of this list. They are recorded in GP records as place of birth and are the best way of case finding | Thank you for your comment. This group will be covered within the population specified in the guideline. Case finding is not within the scope of this guideline, however the NICE Public Health Guidance for hepatitis B and C scope section **4.2.1 (g)** will be including case finding strategies. |
| SH | Department of Health: National Liver Disease Strategy | 8.2 | 3.3.1 | It is important to consider laboratory virology services as this has been a problem. There is merit in specifying requirements for these. I think it is also important to link up viral services – for initial testing all those tested for B should also be tested for C and vice versa. | Thank you for your comment. This is referred to in section 2.2 (a) of the scope. The scope does not include initial diagnostic tests for chronic hepatitis B. |
| SH | Department of Health: National Liver Disease Strategy | 8.3 | 3.3.1b | It is important here to specify what is considered a specialized service. This causes a great deal of confusion in referral pathways. Our information is | Thank you for your comment. Liaison between service departments is not within our remit, but these types of issues can be addressed by the NICE |

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| | | | | that ID services do not always evaluate liver disease and Gastroenterology services are not always specialised enough to consider hepatitis B. Its treatment has become more complicated and I would favour some commissioning 'nudge' to make ID and Liver services work more closely together on this. | implementation team on publication of the guidance. |
| SH | Department of Health: National Liver Disease Strategy | 8.4 | 3.3.1f | HBsAg is also an endpoint (as mentioned later at 3.4.c) | Thank you for your comment, this has been noted and the scope has been amended to reflect this. |
| SH | Department of Health: National Liver Disease Strategy | 8.5 | 3.3.2 | Our strategy groups strongly recommended case finding as the best way of identifying people with chronic hepatitis B and intervening to prevent progression. I am surprised at its omission here | Thank you for your comment. Case finding strategies is already covered in section 4.2.1 (b) and (e) ofthe scope of the NICE Public Health guidance for Hepatitis B and C which is due to be published in December 2012. |
| SH | Department of Health: National Liver Disease Strategy | 8.6 | 3.4 | You mention at the very beginning that many identified cases are not referred to specialized services. Therefore one positive outcome would be measuring the proportion who are referred. | Thank you for your suggestion. However, this outcome will not be included in the guideline development. |
| SH | Royal College of Nursing | 9.0 | General | The Royal College of Nursing welcomes proposals to develop this guideline. The draft scope seems comprehensive. | Thank you for your comment. |
| SH | Royal College of Nursing | 9.1 | General | Need specific guidance re contact tracing with sexual transmission of Hepatitis B virus (HBV) as this is often a grey area as to whether this should be performed via GP, secondary care or Public Health. | Thank you for your comment. This area is covered in the 'Immunisation against infectious disease (The Green Book) - 2006 updated edition'. |
| SH | Royal College of Nursing | 9.2 | 3.1.2 a | Liver transplantation should be considered with recommendations for management of the HBV-infected Liver Transplant candidate or recipient inclusive of pre and post transplant strategies to prevent disease recurrence. | Thank you for your comment.<br>People who had a liver transplant are excluded because it is a very small group due to highly effective preventative treatment. According to the British Liver Trust there were only 663 liver transplants in the UK and the three most common causes were alcohol abuse, hepatitis C and primary |

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| | | | | | biliary cirrhosis (not associated with hepatitis B). Because of this, we did not feel this area was a high priority to consider given the time and resource available. |
| SH | Royal College of Nursing | 9.3 | 3.3.1 c | It will be very useful to include non-invasive methods of assessing liver fibrosis. | Thank you for your suggestion. This area is already included in the scope. |
| SH | Royal College of Nursing | 9.4 | 3.3.1 f | Hepatocellular carcinoma (HCC) surveillance in the non-cirrhotic cohort needs to be addressed in conjunction with the cirrhotic group. | Thank you for your suggestion. This area is already included in the scope. |
| SH | Royal College of Nursing | 9.5 | 3.4 b | How will regression of fibrosis stage be measured as an outcome? Through non-invasive methods?<br><br>If so, consideration needs to include availability of these methods. | Thank you for your comment. Regression of fibrosis stage will be measured by serial liver biopsy or serial non invasive methods. |
| SH | Royal College of Paediatrics and Child Health | 10.0 | General | The College suggests that people co-infected with other sexually transmitted infections should be included. For example, it is increasingly common to see syphilis in some at risk groups. | Thank you for your comment. Individuals co-infected with syphilis and hepatitis B represents a small proportion of people with chronic hepatitis B and will be covered under the general population of this scope. |
| SH | Royal College of Paediatrics and Child Health | 10.1 | 2.1 a | We note a grammatical error: "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." | Thank you for your comment. The scope has been amended. |
| SH | Royal College of Paediatrics and Child Health | 10.2 | 2.2 a | We note a possible error: "and antibodies to hepatitis B surface antigen (HBeAb)". Should this instead read, "HBsAb"? | Thank you for your comment. The scope has been amended. |
| SH | United Kingdom Clinical Pharmacy Association (UKCPA) | 12.0 | 3.3.1 e | Emtricitabine should not be considered as monotherapy as current practice only uses it in combination with tenofovir (Truvada) and should be considered as combination. | Thank you for your comment. We are only considering this drug in combination with Tenofovir (Truvada) and the scope has been amended to reflect this. |

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| SH | United Kingdom Clinical Pharmacy Association (UKCPA) | 12.1 | General | Review co-opted position of pharmacy for this clinical guidance.<br>It is essential that pharmacy is represented at all meetings as pharmacists are increasingly running Hepatitis clinics throughout the NHS and as independent prescribers they are looking after their own clinical case load. Pharmacists are involved in local protocol development, the reviews of introduction of drugs into the trust, and research protocols for this disease area. | Thank you for your comment. We will ensure that pharmacist representation is present for all relevant meetings. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13 | 3.1.1 a | Add as patient group 'patients with end stage kidney disease' This group needs to be specifically mentioned in the scoping exercise (along with those mentioned already under 3.1.1 a) as need special consideration/scoping for drug dosing/combination/interaction | Thank you for your comment. We have stated all people with hepatitis B are included other than those who are specifically excluded rather than list all subgroups. This group will be included within the population. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13.1 | 3.1.1 a | Third bullet should include neonates born to infected mothers. | Thank you for your comment. The guideline will refer to 'Immunisation against infectious disease (Green Book) – 2006 updated edition', as appropriate but will cover assessment and management of neonates. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13.2 | 3.2 | Add 'Opportunistic testing in non NHS community setting'. Non invasive samples (dried blood spots) have been successfully used to test Sheffield Chinese community outside of NHS setting…… | Thank you for your comment. This area is outside the scope<br>Section 4.2.1 (c) of the Scope of the NICE Public Health guidance on hepatitis B and C will address the issue of barriers to testing for groups at most risk of chronic Hepatitis B |
| SH | Sheffield Teaching Hospitals NHS Foundation | 13.3 | 3.3.1 | Identification and assessment of chronic hepatitis B<br>There is no mention of: | Thank you for your comment. Initial diagnosis of hepatitis B will not be covered by this guideline. |

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| | Trust | | | -minimum diagnostic criteria and baseline hepatitis B markers ( as HBV DNA, genotype, resistance, HB eAg/eAb, anti HBc IgM and total anti HBc) for laboratory diagnosis of chronic hepatitis B - scoping exercise should include these and also whether the confirmation (not screening tests) should be in specialist virology laboratory.<br>-use of non invasive samples (dried blood spot and oral fluids) testing for diagnosis of HBV infection. | These tests are described in section 2.2(a) of the scope. Screening tests are outside of the guideline remit. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13.4 | 3.3.1 f | Should include quantitative HBsAg testing as a bullet point.<br>Also 4th bullet<br>'stopping points for treatment according to HBeAg status 'should perhaps be replaced by ' HBV markers ( HBeAg, HBV DNA, HbsAg) as stopping points for treatment. | Thank you for your comment. We agree on both comments and the scope has been amended to reflect these. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13.5 | 3.4 | Logical that point c) should follow point a) in 3.4 . | Thank you for your comment. The scope has been amended to reflect this. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13.6 | 4.1.1 e | Add 'on and off treatment' at the end of the sentence so the 4.1.1 e reads '<br>Monitoring of stage of chronic hepatitis B including timing and frequency of tests on and off treatment. | Thank you for your comment. The scope has been amended to reflect this. |
| SH | Sheffield Teaching Hospitals NHS Foundation Trust | 13.7 | 4.1.1 d | To read :<br>d) Pharmacological treatment for management of chronic hepatitis B including sequential and combination therapies for specific populations and co-infected patients (e.g with HIV, HCV, HDV). | Thank you for your comment. This was not an area prioritised for inclusion following the scoping exercise. There is guidance already available on Hepatitis B in people co-infected with HIV produced by the British Association for Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA). |

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| SH | Infection Prevention Society | 14 | General | A comprehensive document which seems to cover the topic areas. | Thank you for your comment. |
| SH | Roche | 15.0 | 2.1 a | The figure of 180,000 people suffering from chronic hepatitis B comes from a 2002 report. The Rising Curve Report (http://www.hepb.org.uk/information/resources/rising_curve_chronic_hepatitis_b_infection_in_the_uk/rising_curve.pdf ), published in 2007 by the Hepatitis B Foundation, provides a new estimate of 326,000 Chronic Hepatitis B sufferers; this higher estimate is mainly attributed to immigration. | Thank you for your comment. The scope is citing Health Protection Agency data. |
| SH | Roche | 15.1 | 2.1 e | It is stated "*Treatment…aims to reduce viral load*", however there should be consideration in this section that the ultimate treatment goal should be to achieve surface antigen (HBsAg) loss which is generally accepted as a cure (Brunetto, Hepatology, 2009). HBsAg loss reduces the risk of hepatocellular carcinoma (HCC) (Yang et al, New Eng Jnl Med, 2002) and improves patient survival (Fattovich et al, Am J Gastro, 1998). In the absence of surface antigen loss, sustained immune control off treatment and hepatitis B virus (HBV) DNA suppression are the desired treatment outcomes. | Thank you for your comment. This has been noted and the scope has been amended to reflect this. |
| SH | Roche | 15.2 | 2.1 f | It is stated that early studies suggest "*nucleoside or nucleotide analogue treatments… have the most potent effect on viral loads and liver histology, and are likely to have the greatest impact on complications".* Sonneveld et al (Liver International, 2011) question the off-treatment durability of response of the new more potent nucleoside analogues (NAs) and state that long-term or life-long therapy is the only likely outcome when using this class of drugs. By contrast, a licensed, fixed-duration course of treatment with pegylated interferon offers a | Thank you for your comment. We will take this into consideration during the development of the guideline. |

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| | | | | chance of sustained immune control which negates the need for life-long treatment with NAs. | |
| SH | Roche | 15.3 | 2.2 d | Pegylated interferon (peg-IFN) suppresses the virus in a smaller proportion of patients than NAs, however it offers higher rates of HBeAg seroconversion (sustained immune control) which is considered a durable off-treatment response peg-IFN treated HBeAg positive patients, with high rates of surface antigen loss seen subsequently in this patient group (Lau et al, APASL 2009).<br><br>In the HBeAg negative patient group, treatment with peg-IFN has been associated with 5 year post-treatment surface antigen loss rates of 12 per cent, irrespective of a patient's hepatitis B genotype (Marcellin, EASL 2009). Recent data in peg-IFN-treated patients support the monitoring of HBsAg decline from baseline at 12 and 24 weeks in parallel with HBV DNA; this approach allows patients who demonstrate a good off-treatment response to continue on therapy, whilst poor responders can be stopped early (Rijckborst et al, Hepatology, 2010).<br><br>A response guided therapy (RGT) algorithm with peg-IFN treatment allows for individualised and cost-effective healthcare in a group of patients whose only treatment option has historically been lifelong suppression of HBV DNA with NA therapy. | Thank you for your comment, this has been noted.<br><br>We will be considering this in context of HBsAg quantification in an earlier part of the scope. |
| SH | Roche | 15.4 | 2.2 l | The SPC recommend dose and duration of 180 micrograms once weekly for 48 weeks was confirmed as the most efficacious and beneficial for HBeAg-positive patients compared with shorter durations and lower doses due to the high rates of HBeAg seroconversion (NEPTUNE Study, EASL, | Thank you for your comment. |

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| | | | | 2011).<br><br>In HBeAg negative disease a RGT strategy should be considered where all HBeAg negative patients are given a minimum of 12 weeks of peg-IFN first before then being considered a candidate for lifelong NA therapy based on their decline in HBsAg titres and HBV DNA decline. | |
| SH | Roche | 15.5 | 3.3.1 | HBsAg quantification testing should to be considered as a routine HBV test as this will help clinicians to ascertain the stage of disease of each individual patient prior to treatment and will allow HBeAg negative patients to be managed with peg-IFN as part of a RGT strategy (Brunetto, Hepatology, 2010). | Thank you for your comment. The scope has been amended to reflect this. |
| SH | Roche | 15.6 | 3.3.1 f | In relation to the bullet point "stopping points for treatment according to HBeAg status":-<br><br>RGT requires HBsAg quantitative testing at baseline and then at weeks 12, 24, 48 in HBeAg negative patients being treated with peg-IFN. | Thank you for your comment. We will take this into consideration during the development of this guideline. |
| SH | Roche | 15.7 | 3.4 | Sustained immune control (HBeAg seroconversion in HBeAg positive patients and HBV DNA <10,000 copies/ml in HBeAg negative patients) is another relevant outcome in the context of Peg_IFN treatment, since HBsAg loss can be achieved through off-treatment sustained immune control following peg-IFN. | Thank you for your comment, this has been noted. Aspects of sustained immune control are already included in the outcomes. |
| SH | Roche | 15.8 | 3.5 | The above appears to have been considered by the Institute, by their acknowledgment in the Draft Scope that stopping rules should be considered. It is worth noting, however that RGT with a 12 week stopping rule in HBeAg negative patients has not been considered in previous NICE appraisals. Hence when identifying the most cost-effective strategy for | Thank you for your comment, this has been noted and we will take this into consideration when developing the guideline. |

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| | | | | the treatment of HBeAg negative patients, upfront RGT with peg-IFN should be included as a comparator / intervention. | |
| SH | Roche | 15.9 | 4.1.1 e | As per our previous comments, HBsAg quantitative testing is a key tool in the assessment and management of chronic hepatitis B. | Thank you for your comment, this has been noted and the scope has been amended to reflect this. |
| SH | Bristol-Myers Squibb Pharmaceuticals | 16.0 | 2.2 | Tenofovir in combination with emtricitabine is used off label, never registered or endorsed by NICE. | Thank you for your comment. Recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. |
| SH | Bristol-Myers Squibb Pharmaceuticals | 16.1 | 3.1.1. | During the scoping workshop it was agreed to reformulate this as: "Everybody with chronic hepatitis B infection with the exception of liver transplant (to be covered elsewhere)" | Thank you for your comment. We considered the wording of the scope following the stakeholder workshop and we believe that the wording of the defined population is detailed and informative. |
| SH | Bristol-Myers Squibb Pharmaceuticals | 16.2 | 3.3.1. | We would like to note that it has been NICE's policy to endorse only licensed indications. We expect that this would not change.<br>All adverse events should be considered equally, not only renal toxicity as the most important one | Recommendations will normally fall within licensed indications; exceptionally and only if clearly supported by evidence, use outside a licensed indication may be recommended. |
| SH | Bristol-Myers Squibb Pharmaceuticals | 16.3 | 5 | We noted that there is a visible emphasis on combinations and sequential therapy. There is no RCT data what so ever to prove that any of these could work and they are not licensed indications for these compounds. | Recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. (http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp) |
| SH | Royal College of Physicians (RCP) | 17.0 | General | The RCP is grateful for the opportunity to respond to the above consultation. We believe that the scope should also emphasise the importance of HIV testing | Thank you for your comment. This was not an area prioritised following the scoping exercise. There is guidance already available on Hepatitis B in people |

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| | | | | in patients. | co-infected with HIV produced by the British Association for Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA) |

**These organisations were approached but did not respond:**

Advisory Group on Hepatitis

Alder Hey Children's NHS Foundation Trust

Association of British Health-Care Industries

Barchester Healthcare

Barnsley Hospital NHS Foundation Trust

Birmingham Childrens Hospital NHS Foundation Trust

BMJ

British HIV Association (BHIVA)

British Medical Association (BMA)

British National Formulary (BNF)

British Paediatric Allergy, Immunity & Infection Group

British Psychological Society, The

British Renal Society

British Society of Gastroenterology

British Transplantation Society

Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)

Care Quality Commission (CQC)

Central Lancashire PCT

Central North West London NHS Trust

Connecting for Health

Department for Communities and Local Government

Department for Education

Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

Department of Health, Social Services & Public Safety, Northern Ireland (DHSSPSNI)

East Cheshire NHS Trust

Faculty of Occupational Medicine

Frontier Therapeutics Limited

George Eilot Hosptal Trust

Gilead Sciences Ltd

Gloucestershire Hospitals NHS Trust

Great Western Hospitals NHS Foundation Trust

Greater Manchester West Mental Health NHS Foundation Trust

Haag-Streit UK

Haemophilia Society, The

Healthcare Improvement Scotland

Healthcare Quality Improvement Partnership

Hepatitis B & C: Ways to promote and offer testing Programme Development Group

Letterkenny General Hospital

Luton & Dunstable Hospital NHS Foundation Trust

Medical Foundation for AIDS & Sexual Health (MedFASH)

Medicines and Healthcare Products Regulatory Agency (MHRA)

Ministry of Defence (MoD)

National Kidney Federation (NKF)

National Patient Safety Agency (NPSA)

National Treatment Agency for Substance Misuse

National Users Network

NETSCC, Health Technology Assessment

NHS Clinical Knowledge Summaries Service (SCHIN)

NHS Direct

NHS Hertfordshire

NHS Hertfordshire

NHS Plus

NHS Sheffield

NHS Western Cheshire

North Tees & Hartlepool NHS Foundation Trust

Northumberland, Tyne & Wear NHS Foundation Trust

Nottingham University Hospitals NHS Trust

PROGRESS

Public Health Wales

RioMed Ltd.

Rotherham NHS Foundation Trust

Royal Berkshire NHS Foundation Trust

Royal College of Anaesthetists

Royal College of General Practitioners Wales

Royal College of Midwives

Royal College of Pathologists

Royal College of Psychiatrists

Royal College of Radiologists

Royal College of Surgeons of England

Royal Pharmaceutical Society of Great Britain

Royal Society of Medicine

Scottish Intercollegiate Guidelines Network (SIGN)

Social Care Institute for Excellence (SCIE)

South East Coast Ambulance Service

Teva UK Limited

Wales Viral Hepatitis Management Group

Welsh Assembly Government

Welsh Scientific Advisory Committee (WSAC)

West Midlands Ambulance Service NHS Trust

Wirral University Teaching Hospital NHS Foundation Trust

York Teaching Hospital NHS Foundation Trust