NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA96; Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B, TA154; Telbivudine for the treatment of chronic hepatitis B, TA153; Entecavir for the treatment of chronic hepatitis B and TA173; Tenofovir disoproxil fumarate for the treatment of hepatitis B

TA96 – guidance was issued in February 2006. The original review date was February 2007, at which time it was decided to defer the review proposal until the outcomes of TA153 and TA154 were known.

TA154 – guidance was issued in August 2008. The original review date was February 2009.

TA153 – guidance was issued in August 2008. The original review date was February 2009.

In May 2009, there was insufficient new evidence that would materially affect the recommendations in TA96, TA153 and TA154. It was decided to defer the review proposal until March 2012 so that results from ongoing clinical trials comparing combination versus monotherapy for hepatitis B would be available.

TA173 – guidance was issued in July 2009. Review date is March 2012.

Background

At the GE meeting of 19 July 2011 it was agreed we would consult on the review plans for this guidance. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

Proposal put to consultees:	NICE has been asked to develop a clinical guideline and quality standard on the diagnosis and management of hepatitis B. These projects overlap with the technology appraisals listed above. It is proposed that the technology appraisals are included in the guideline as follows: • **TA153, TA154, TA173 and recommendation 1.1 of TA96** – These recommendations will be incorporated, verbatim, into the clinical guideline. The technology appraisals will be moved to the static list and will remain extant when the guideline is published. This has the consequence of preserving the funding direction for TA153. TA173 and recommendation 1.1 of TA96. The guideline will contextualise this guidance by considering the place of the recommended options within treatment sequences and combination drug regimens. • **Recommendations 1.2–1.4 of TA96** – These recommendations will be updated by the clinical guideline and will be withdrawn when it is published.

Rationale for selecting this proposal	These technology appraisals overlap with the remit of an ongoing clinical guideline and quality standard. Taken together, the guidance recommends peginterferon alfa an option for the initial treatment of adults with chronic hepatitis B and entecavir or tenofovir disoproxil as options when antiviral treatment is indicated. Telbivudine is not recommended, while adefovir dipivoxil is recommended only in certain circumstances. TA96 was conducted as a multiple technology appraisal (MTA) and the each of the subsequent appraisals was conducted as a single technology appraisal (STA) so the options have never been fully compared with each other and it is not clear at present which of the antiviral drug options should be chosen first, and which should be reserved for second or subsequent line therapy. It is intended that the question of using antiviral drugs within treatment sequences (including those that have been recommended as options by the relevant technology appraisals) will be addressed by the clinical guideline. The guideline will also consider the role of combination regimens of antiviral drugs. The recommendations of TA153, TA154, TA173 and recommendation 1.1 of TA96 can be incorporated into the guideline while allowing for further guidance to be given on the appropriate use of the recommended options within treatment sequences and combination regimens. However, recommendations in TA96 on adefovir dipivoxil define the place of adefovir dipivoxil in a sequence and have been rendered obsolete by the subsequent technology appraisals, so these recommendations will be updated by the guideline. This review proposal was prepared taking into account the principles outlined in the Department of Health policy document PWG IB (10)05.

GE is asked to consider the original proposal in the light of the comments received from consultees and commentators, together with any responses from the appraisal team. It is asked to agree on the final course of action for the review.

Recommendation post consultation:	The technology appraisals will be included in the guideline as follows: • **TA153, TA154, TA173 and recommendation 1.1 of TA96** – These recommendations will be incorporated, verbatim, into the clinical guideline. The technology appraisals will be moved to the static list and will remain extant when the guideline is published. This has the consequence of preserving the funding direction for TA153. TA173 and recommendation 1.1 of TA96. The guideline will contextualise this guidance by considering the place of the recommended options within treatment sequences and combination drug regimens. **Recommendations 1.2–1.4 of TA96** – These recommendations will be updated by the clinical guideline and the technology appraisal recommendations will be withdrawn when the guideline is published.

Respondent	**Response to proposal**	**Details**	**Comment from Technology Appraisals**
Healthcare Improvement Scotland	No comment	Healthcare Improvement Scotland has no comment to make on the proposals regarding TAs 96, 154, 153 and 173	No action required
British HIV Association	Neither agree nor disagree	BHIVA has been trying to contact NICE to establish whether this proposed clinical guideline will include HIV coinfection but the final decision remains unclear. From a BHIVA viewpoint it is essential that the following be included in any new guideline on these agents whether this be within the existing guidelines if rewritten or within the new proposed clinical guideline: 1. All patients with hepatitis B are tested for HIV 2. All patients commencing these agents are retested for HIV if have been at risk of acquisition since initial test 3. Initiation of therapy within any agent should only be performed after discussion with the HIV treating	The current technology appraisal guidance does not apply to people with chronic hepatitis B known to be co-infected with hepatitis C, hepatitis D or HIV. Any recommendations relating to HIV testing are outside the remit of this technology appraisal

Respondent	Response to proposal	Details	Comment from Technology Appraisals
		physician 4. If co-infected guidance is to be issued within this guideline for these drugs or within the clinical guidelines that close collaboration is sought with BHIVA who will be issuing new co-infected hepatitis B guidelines in 2012 to ensure that there is agreement and that an HIV/Hepatitis B coinfection expert is included or co-opted to the panel	
British Liver Trust	Agree	We would be pleased that a clinical guideline for the treatment of hep b is issued. We would ask that clinical guidance is also detailed to allow the treatment regimens of these drugs to be prescribed by their proven effectiveness, so the appropriate treatment is offered to each patient.	No action required
Royal College of Pathologists	No comment	The Royal College of Pathologists has no comments to make on the above review proposal	No action required
Royal College of Nursing	No comment	Nurses working in this area of health have reviewed the above mentioned NICE Technology appraisal guidance no.'s 96, 153 and 173. There are no comments or evidence to submit at this stage on behalf of the Royal College of Nursing.	No action required
Royal College of Physicians / British Association for	Neither agree nor disagree	The Royal College of Physicians (RCP) is grateful for the opportunity to respond to the above proposal consultation. In preparing a response we have liaised with the British Association for Sexual Health & HIV (BASHH) and would like	The technology appraisal guidance does not apply to people with chronic hepatitis B known to be co-infected with

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Sexual Health and HIV		to offer the following comments. Our experts believe that it is essential that the following be included in any new guideline on these agents; whether this be within the existing guidelines, if rewritten, or within the new proposed guidelines. 1 All patients with hepatitis B are tested for HIV 2 All patients commencing these agents are retested for HIV if they have been at risk of acquisition since initial test 3 If coinfected guidelines are to be issued within this guideline for these drugs we would advocate close collaboration with the British HIV Association (BHIVA) who will be issuing new coinfected hepatitis B guidelines in 2012. We would also strongly advise that an HIV/Hepatitis B coinfection expert is included or coopted to the panel to ensure that treatment is looked at in co-infection with HIV.	hepatitis C, hepatitis D or HIV. Any recommendations relating to HIV testing are outside the remit of this technology appraisal.
Bristol-Myers Squibb	Agree	We agree that it is clear that sufficient new evidence has emerged for the Appraisal Committee to be asked to undertake a full appraisal review. However, in order to de compliant with the best use of the institute resources, we agree that they should be included on the clinical guidelines. After looking at the guidance and the possible scope for a review, we believe that this topic would be better dealt with within the context of a clinical guideline. We totally agree that the recommendations from TA153, TA154, TA173 and recommendation 1.1 of TA96 be incorporated, verbatim, into the ongoing clinical guideline on ‘The diagnosis and	No action required

Respondent	Response to proposal	Details	Comment from Technology Appraisals
		management of hepatitis B in children, adolescents and adults'. It would be appropriate for the technology appraisals will be moved to the static list and will remain extant when the guideline is published. We agree that keeping the funding direction for TA153, TA173 and recommendation 1.1 of TA96 would be the most sensible way to proceed.	
Gilead Sciences	Agree	I can confirm that Gilead support your proposal to incorporate updates to the Hepatitis TA's by way of a clinical guideline. We welcome the opportunity to support NICE in the development of this guideline. Furthermore, we note the comments based on assessment of implementation and would be happy to discuss the implementation of TA173. We appreciate that due to tenofovir being licenced for more than one therapy area can make interpretation of uptake quite challenging.	No action required
British Society of Gastroenterology	Agree	I would support incorporation of previous TAGs into the guideline, I do not feel that the evidence base has changed significantly and that a further review is required at present.	No action required

No response received from:

Manufacturers/sponsors	General
• Novartis Pharmaceuticals UK (telbivudine) • Roche Products (peginterferon alfa-2a)	• Board of Community Health Councils in Wales • British National Formulary • Care Quality Commission • Commissioning Support Appraisals Service

Patient/carer groups

- Afiya Trust
- Alliance
- AVERT
- Black Health Agency
- British Organ Donor Society (BODY)
- Chinese National Healthy Living Centre
- Compass UK
- Counsel and Care
- Drugs Action
- Drugscope
- Equalities National Council
- GMFA - The Gay Men's Health Charity
- Haemophilia Alliance
- Haemophilia Society
- Hepatitis A –Z
- Hepatitis B Foundation UK
- Muslim Council of Britain
- Muslim Health Network
- NAM Publications
- National AIDS Trust
- Positively UK
- South Asian Health Foundation
- Specialised Healthcare Alliance
- Terrence Higgins Trust
- Transplant Support Network
- Youth Net

Professional groups

- Association of Clinical Microbiologists
- Department of Health, Social Services and Public Safety for Northern Ireland
- Medicines and Healthcare products Regulatory Agency
- National Association of Primary Care
- National Pharmacy Association
- NHS Alliance
- NHS Commercial Medicines Unit
- NHS Confederation
- Public Health Wales NHS Trust
- Scottish Medicines Consortium

Possible comparator manufacturer(s)

- Glaxosmithkline (lamivudine)
- Merck Sharpe and Dohme (interferon alfa-2b, peginterferon alfa-2b)

Relevant research groups

- Centre for Sexual Health & HIV Research
- Cochrane Hepato-Biliary Group
- Cochrane Infectious Diseases Group
- Foundation for Liver Research
- MRC Clinical Trials Unit
- National Institute of Health Research
- Research Institute for the Care of Older People

Assessment Group

- Assessment Group tbc
- National Institute for Health Research Health Technology Assessment Programme

• Association of Nurses in Substance Abuse • Association of Surgeons of Great Britain and Ireland • British Association for Services to the Elderly • British Association for the Study of the Liver • British Geriatrics Society • British Infection Association • British Liver Nurses Forum • British Transplantation Society • British Viral Hepatitis Group • European Association for the Treatment of Addiction UK • Haemophilia Nurses Association • Health Protection Agency • Hepatitis Nurse Specialist Forum • Infection Control Nurses Association • Medical Foundation for AIDS & Sexual Health • Royal College of Anaesthetists • Royal College of General Practitioners • Royal College of Surgeons • Royal Pharmaceutical Society • Royal Society of Medicine • Society for General Microbiology • United Kingdom Clinical Virology Network • United Kingdom Clinical Pharmacy Association • United Kingdom Haemophilia Centre Doctors' Organisation <u>Others</u> • Department of Health • Heart of Birmingham Teaching Primary Care Trust • NHS Blackburn with Darwen Teaching Care Trust • Welsh Government	<u>Associated Guideline Groups</u> • National Clinical Guidelines Centre <u>Associated Public Health Groups</u> • tbc

GE paper sign-off: Janet Robertson, Associate Director – Technology Appraisals Programme

Contributors to this paper:

Technical Lead: Christian Griffiths

Project Manager: Andrew Kenyon

28 September 2011