NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Bulevirtide for treating chronic hepatitis D

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of bulevirtide within its marketing authorisation for treating chronic hepatitis D.

Background

Hepatitis D, also known as hepatitis Delta, is an infectious disease of the liver caused by the hepatitis D virus (HDV). It only affects people infected with hepatitis B, as it needs the hepatitis B virus (HBV) to be able to survive in the body. Infection may be acquired along with HBV (co-infection) or after HBV infection (superinfection). Similarly to hepatitis B, it usually spreads through blood-to-blood contact or sexual contact. It is also transmitted from mother to child during birth and delivery. Chronic HDV/HBV infection is the most severe form of viral hepatitis, with an increased risk of cirrhosis, liver decompensation, hepatocellular carcinoma and mortality.[1]

The majority of people infected with HBV during adulthood make a full recovery and acquire immunity from future infection. Less than 5% of infected adults will develop chronic hepatitis B, defined as viraemia and hepatic inflammation that persists for more than 6 months after acute infection with HBV.[2] Cirrhosis can progress to become 'decompensated', where the remaining liver can no longer compensate for the loss of function. There is an increased risk of hepatocellular carcinoma among people with chronic hepatitis B and cirrhosis.[3] The World Health Organisation estimated, that at least 5% of people with chronic HBV infection are co-infected with HDV, resulting in a total of 15 to 20 million persons infected with HDV worldwide.[4] However, the percentage can be higher as not all people with HBV infection get tested for HDV. A retrospective analysis of 962 patients, referred to Kings' College Hospital in South London between 2000 to 2006 with HBV, showed that 8.5% tested positive for HDV antibodies.[5] The Hospital Episode Statistics for England 2018/19 recorded 21 admissions and 26 finished consultant episodes for chronic viral hepatitis B with D virus infection (ICD-10 code B18.0). While 496 admissions and 427 finished consultant episodes were recorded for chronic viral hepatitis B without D virus infection (ICD-10 code B18.1).[6]

The aim of treatment is to prevent transmission, cirrhosis, hepatocellular carcinoma and liver failure. Clinical guidance 165, recommends a 48-week course of peginterferon alfa-2a for people co-infected with chronic hepatitis B and hepatitis D infection who have evidence of significant fibrosis (METAVIR stage greater than or equal to F2 or Ishak stage greater than or equal to 3).

The technology

Bulevirtide (Hepcludex, MYR Pharmaceuticals) is an HBV/HDV entry inhibitor that binds and blocks the jointly used sodium taurocholate co-transporting polypeptide (NTCP) receptor on liver cells. It misdirects HBV and co-infecting HDV to an unproductive pathway and prevents an infection of the cell. Bulevirtide is delivered subcutaneously.

Bulevirtide has a marketing authorisation in the UK for the treatment of chronic HDV infection in plasma (or serum) HDV-RNA positive adult patients with compensated liver disease.

Intervention(s)	Bulevirtide
Population(s)	Adults with chronic hepatitis D who have compensated liver disease.
Comparators	• Best supportive care • Peginterferon alfa-2a
Outcomes	The outcome measures to be considered include: • virological response • biochemical response • sustained response • development of resistance to treatment • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of bulevirtide is conditional on the presence of HDV. The economic modelling should include the costs associated with diagnostic testing for HDV in people with hepatitis B who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.

Other considerations	If the evidence allows the following subgroups will be considered: • severity of the disease. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Tenofovir alafenamide for treating chronic hepatitis B (2017) NICE Technology Appraisal 435. Terminated appraisal. Tenofovir disoproxil for the treatment of chronic hepatitis B (2009). NICE Technology Appraisal 173. Guidance on static list Telbivudine for the treatment of chronic hepatitis B (2008). NICE Technology Appraisal 154. Guidance on static list Entecavir for the treatment of chronic hepatitis B (2008). NICE Technology Appraisal 153. Guidance on static list Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B (2006). NICE Technology Appraisal 96. Guidance on static list. Related Guidelines: Hepatitis B (chronic): diagnosis and management (2013) NICE guideline CG165 Related Quality Standards: Hepatitis B (2014) NICE quality standard 65 Related NICE Pathways: Hepatitis B (chronic) (2020) NICE pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Manual for Prescribed Specialised Services 2018/19. Chapter 65, Highly specialist services for adults with infectious diseases Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

References

1. Mentha, N., Clément, S., Negro, F., & Alfaiate, D. (2019). A review on hepatitis D: From virology to new therapies. Journal of advanced research; 17, 3-15.

2. World Health Organisation (2019) Guidelines for the prevention, care and treatment of person with chronic hepatitis B infection Accessed February 2020.

3. Oakes K (2014) Chronic hepatitis B, part 1: hepatitis B: prevalence and pathophysiology. Nursing Times; 110: 7, 12-16.

4. World Health Organisation (2019) Hepatitis D Accessed February 2020.

5. Cross, T. J., Rizzi, P., Horner, M., Jolly, A., Hussain, M. J., Smith, H. M., Vergani, D., & Harrison, P. M. (2008). The increasing prevalence of hepatitis delta virus (HDV) infection in South London. Journal of medical virology; 80: 2, 277-282.

6. NHS (2019) Hospital Admitted Patient Care Activity 2018-19 Accessed February 2020.