British Infection Society: Response to the Appraisal Consultation Document on Telbivudine

The British Infection Society

The British Infection Society is a charitable organisation representing 950 professionals (the majority being infectious disease physicians and microbiologists) working in the field of infection. Many of our members are directly involved in the management of and research into chronic hepatitis B infection. The comments below reflect a consensus view from those members with particular expertise and experience in the area of hepatitis B.

General comments on the STA

This STA examines the utility and cost effectiveness of telbivudine for the monotherapy of chronic hepatitis B infection. It is the view of the BIS that such appraisals, while helpful in some respects, are of limited value. We believe that there should be a more general appraisal of the management of chronic hepatitis B infection, taking into account not only the individual drugs available, but also considering treatment strategies (interferon versus antiviral drugs, combination therapy versus monotherapy), and the cost effectiveness of patient stratification using genotyping. We recognise that this would be a difficult undertaking. The decisions involved would be complex, and there is a lack of data to support some analyses. However we would encourage NICE to consider a wide ranging assessment of the overall management of chronic hepatitis B infection as its next step.

Comments on the ACD

i) We are not aware of any important data on telbivudine which has been excluded from the appraisal, although the virological evidence regarding resistance has not been presented in any detail.

ii) Telbivudine is, like lamivudine, a nucleoside analogue reverse transcriptase inhibitor of HBV replication. Resistance to telbivudine is mediated by mutations at 181T and 204V/I on the polymerase gene, the same mechanism as lamivudine resistance. Clinical studies have shown a 22% telbivudine resistance rate after 2 years treatment. This was lower than the rate seen for lamivudine in the same trial (although similar to that reported for lamivudine in other trials). However telbivudine resistance is likely to increase in at least a linear fashion year on year. In a disease in which treatment will continue for many years, or possibly for life, these levels of resistance are completely unacceptable. Given the availability of drugs with much lower rates of resistance, neither lamivudine nor telbivudine should be used as monotherapy in treatment naive HBV infected patients. In addition any virus which is already resistant to lamivudine is likely to have decreased susceptibility to telbivudine, making the latter unsuitable as second line therapy.

iii) Regardless of economic modelling, the pattern of genotypic mutations that is seen in hepatitis B virus exposed to telbivudine (and which confers resistance to the drug, and cross-resistance to other drugs) make it unsuitable as a first line agent for monotherapy in chronic HBV. However it is a potent antiviral drug, and may have a role when given in combination with another agent; this remains to be addressed through further research.

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