July 28, 2024

Treating Hepatitis B: Hepatitis B Foundation Position Statement

Hepatitis B Foundation takes the position that all people living with chronic hepatitis B and having any detectable hepatitis B viral DNA in the blood[a], should be considered eligible and offered treatment with currently available therapeutics, if ANY one of the following criteria is met:

1. **They have a family history of cirrhosis or HCC;**
2. **They are older than 30 years of age[b];**
3. **They request treatment[c];**
4. **They have evidence of liver inflammation or liver damage[d];**
5. **They have co-morbidities or other risk factors that support treatment[e].**

*statement notes a,b,c,d,e follow on page 3.

The position statement is intended to buttress the position of other expert organizations, promote the delivery of patient-centered care, simplify and help close current gaps in treatment, and ultimately achieve hepatitis B elimination equitably.

The statement reflects real-world situations where treatment decisions may be influenced by environment, circumstances, and resources. Critically, this statement brings the patient voice and community experience to the table – while remaining supported by science and expert opinion.

Statement Commentary

In 2022, the HBF convened a workshop of 32 experts to consider to what extent, if any, the current standard of care for managing chronic hepatitis B should be modified. The group consisted of hepatologists, primary care practitioners, infectious disease specialists, virologists, public health professionals, and people living with hepatitis B. The consensus was that an expansion of the treatment guidelines should be considered. The HBF developed this position statement in response to that workshop, and consulted over 50 experts clinicians, scientists, and people with lived experience in the crafting of this statement. Those supporting the position are signatories (below).

During development of this statement, there were many opinions regarding specific criteria for treatment eligibility. This included age (thoughts on changing or removing the lower age limit), HBV DNA level (thoughts on changing criteria to HBV DNA >2,000 IU/mL), and the roles of HBeAg, ALT and genotype in treatment eligibility. There was much discussion especially around the acceptable level of HBV DNA to offer antiviral treatment. Ultimately, the decision to include any detectable HBV DNA (versus HBV DNA >2,000 IU/mL) reflects the majority opinion, and the scientific evidence that any viral replication seen in a blood sample reflects increased viral activity taking place in the liver[1].

This HBF position statement is largely consistent with the 2023 published guidelines from the China Medical Association[2], (who used the current body of published literature to make their recommendations, deemed "B" level), as well as our experience with patients and providers.

More background regarding some of the basis of these positions can be found in Roma et al[3] and Wong et al[4].

This statement is not meant to be prescriptive. The statement does not posit that individuals with any detectable HBV DNA should start antivirals based on this recommendation alone. The statement is intended to open up the possibility of treatment initiation for more individuals, based on simple factors related to risk, and removing the need for sometimes hard-to-access tests. When there is access to the full range of tests to stratify risk, those should, of course, be used.

Signed by:

Timothy Block, PhD
Co-founder and Past President, Hepatitis B Foundation and Baruch S. Blumberg Institute
Chairman of the Board, Hepatitis B Foundation

Chari Cohen, DrPH, MPH
President, Hepatitis B Foundation
Professor, Baruch S. Blumberg Institute

Su Wang, MD, MPH, FACP
Director, Center for Asian Health, Saint Barnabas Medical Center
Senior Advisor for Global Health, Hepatitis B Foundation

Robert Gish, MD
Medical Director, Hepatitis B Foundation
Principal, Robert G. Gish Consulting LLC

Kosh Agarwal, BMed Sci (Hons), MD, FRCP
Consultant Hepatologist & Transplant Physician
Institute of Liver Studies
Kings College Hospital, London

Harvey Alter, MD
Former Chief, Infectious Disease Section, Transfusion Medicine, National Institutes of Health

Richard Andrews, MD, MPH
President, Houston Viral Hepatitis Task Force
National Advisory Committee, Hep B United
Past Co-chair, National Task Force on Hepatitis B

Peter Block, MD, MSc
Clinical Fellow
Yale School of Medicine

Carol Brosgart, MD
Clinical Professor of Medicine, Biostatistics and Epidemiology, UCSF
National Advisory Committee, Hep B United
Hepatitis B Foundation Board of Directors

Maria Buti MD, FAASLD
Professor of Medicine and Senior Consultant
Hospital Universitario VAlle Hebron

Jacki Chen, PhD
University Professor, Department of Pharmacology
Rutgers University RWJ School of Medicine
#justB storyteller, Hepatitis B Foundation

Carla Coffin, MD, MSc, FRCPC
Professor of Medicine
Cumming School of Medicine, University of Calgary
Medical Director of the Viral Hepatitis Clinic,
Calgary Division of Gastroenterology and Hepatology,
Department of Medicine, Alberta Health Services

Douglas Dieterich, MD
Professor, Medicine, Liver Diseases
Icahn School of Medicine at Mount Sinai

Geoffrey Dusheiko, MB, BCH, FCP (SA), FRCP (EDIN)
Emeritus Professor of Medicine, UCL Institute of Liver and Digestive Disease, Royal Free University College London School of Medicine

Ahmed Elsharkawy, MD
Consultant Transplant Hepatologist, University Hospitals Birmingham
Honorary Senior Lecturer, University of Birmingham

Lawrence Friedman, MD
Gastroenterologist, Massachusetts General Hospital

Hannah Lee, MD
Associate Professor of Medicine
Virginia Commonwealth University
Stravitz-Sanyal Institute for Liver Disease and Metabolic Health

Patrick Kennedy, MB BCH BAO BMEDSCI FRCP MD
Professor of Translational Hepatology
Consultant Hepatologist
Queen Mary University of London

Philippa Matthews, FRCP, FRCPath, DPhil
Clinical Group Leader, The Francis Crick Institute
Professor of Infectious Diseases, University College London
Honorary Consultant in Clinical Infection, University College London Hospital and Central North West London NHS Foundation Trust

Lefteris Michailidis, PhD
Assistant Professor
Emory University School of Medicine

Devin Razavi-Shearer, MPH
Director, The Polaris Observatory
Center for Disease Analysis Foundation

Homie Razavi, PhD
Founder and Managing Director
Center for Disease Analysis Foundation

Raymond Schinazi, PhD
Francés Winship Walters Professor of Pediatrics and Chemistry
Director, Laboratory of Biochemical Pharmacology
Emory University

John Tavis, PhD
Professor, Molecular Microbiology and Immunology
Saint Louis University School of Medicine

Amy Trang, PhD, MEd
Administrator, National Task Force on Hepatitis B
Founder and CEO, Social Capital Solutions, Inc.

Thomas Tu, PhD
Senior Research Fellow
Westmead Institute for Medical Research (WIMR)
Faculty of Medicine and Health (FMH)

John W. Ward, MD
Director, Coalition for Global Hepatitis Elimination
The Task Force for Global Health

Robert Wong, MD, MS
Clinical Associate Professor of Medicine (Affiliated), Division of Gastroenterology and Hepatology
Veterans Affairs Palo Alto Healthcare System
Stanford University School of Medicine

Statement Notes

a. Viral DNA
   - If DNA testing is not available, treatment decisions can rely upon other factors such as age, family history, medical status, comorbidities and/or patient preference.
   - This is intended to be sensitive and responsive to the difference needs and resources of global communities. Comprehensive evaluation with additional lab tests and investigations to assess risk (i.e. genotype, mutations, viral load) are not discouraged if accessible and not a burden to patients. More nuanced risk assessment can be made according to other guidelines/guidance, but this position statement provides a broader, more inclusive approach to hepatitis B.

- In places where there is little access to birth dose and no access to viral load testing, decisions should err on the side of treating pregnant people.

b. Age
   - In communities where liver cancer occurs in younger people with chronic hepatitis B, and in regions or communities where pediatric prevalence remains relatively high, treatment can be initiated at younger ages, if agreed upon by the provider and patient.
   - In regions where the majority genotype is associated with increased incidence of HCC, treatment should be considered at earlier ages, though we understand that genotyping is less available in low- and middle-income countries.

c. Patient Preference
   - In all circumstances, patient preference must be considered. Patient preference to be treated, or not to be treated, should be respected.
   - Treatment should be based on shared decision making between providers and patients, who should have flexibility to make treatment decisions based upon the specific circumstances in their situation.
   - Patients should be fully informed about risk of progression, treatment criteria, and reasons they are being considered for treatment. This information should be conferred in a way that is reflective of the patient's health literacy and culture.
   - Patients should be fully informed about the importance of following treatment protocol, to work towards improving long-term antiviral adherence.
   - The idea of treatment as prevention – both to prevent liver cancer and to prevent transmission of HBV to others can be used to guide treatment decisions. This should coincide messaging and reassurance about vaccination as the most effective transmission prevention tool. In the development of this position statement, there was some concern about including language on "treatment as prevention," but the majority felt that this statement was important to include.

d. Liver Damage
   - Evidence of liver inflammation, including mild inflammation reflective of elevated ALT, or liver damage, including advanced fibrosis or cirrhosis.

e. Co-infection/superinfection with HIV, HCV, or HDV should be a strong consideration for treatment at any HBV DNA level.

References

1. Pierra Rouviere C, Dousson CB, Tavis JE. HBV replication inhibitors. Antiviral Res. 2020 Jul;179:104815.
2. You H, Wang F, Li T, et al. Guidelines for the Prevention and Treatment of Chronic Hepatitis B (version 2022). *J Clin Transl Hepatol*. 2023;11(6):1425-1442.
3. Roma, K., Hsu, M., Khattak, A. and Gish, R., 2023. Evidence-Based Strategies for Micro-elimination of Chronic Hepatitis B Virus Infection. *Current Hepatology Reports*, *22*(3), pp.118-129.
4. Wong, R.J., Kaufman, H.W., Niles, J.K., Kapoor, H. and Gish, R.G., 2023. Simplifying treatment criteria in chronic hepatitis B: reducing barriers to elimination. *Clinical Infectious Diseases*, *76*(3), pp.e791-e800.