ANNEX 2: Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection – Summary of recommendations

WHO recommendations for the prevention, care and treatment of persons with chronic hepatitis B infection

Non-invasive assessment of liver disease stage at baseline and during follow up:
APRI (aspartate aminotransferase [AST]-to-platelet ratio index) is recommended as the preferred non-invasive test (NIT) to assess for the presence of cirrhosis (APRI score >2 in adults) in resource-limited settings. Transient elastography (e.g. FibroScan) or FibroTest may be the preferred NITs in settings where they are available and cost is not a major constraint.
(Conditional recommendation, low quality of evidence)

Who to treat: As a priority, all adults, adolescents and children with CHB and clinical evidence of compensated or decompensated cirrhosis (or cirrhosis based on APRI score >2 in adults) should be treated, regardless of ALT levels, HBeAg status or HBV DNA levels.
(Strong recommendation, moderate quality of evidence)

Who to treat: Treatment is recommended for adults with CHB who do not have clinical evidence of cirrhosis (or based on APRI score ≤2 in adults), but are aged more than 30 years (in particular), and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL), regardless of HBeAg status.
(Strong recommendation, moderate quality of evidence)

Who to treat: Where HBV DNA testing is not available: Treatment may be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status.
(Conditional recommendation, low quality of evidence)

HBV/HIV coinfected persons: In HBV/HIV-coinfected individuals, a Tenofovir based ART regimen should be initiated in all HIV-infected persons, regardless of stage of liver disease or CD4 count.
(Strong recommendation, low quality of evidence) UPDATED RECOMMENDATION 2015 ARV GUIDELINES

Who not to treat but continue to monitor: Antiviral therapy is not recommended and can be deferred in persons without clinical evidence of cirrhosis (or based on APRI score ≤2 in adults), and with persistently normal ALT levels and low levels of HBV DNA replication (HBV DNA <2000 IU/mL), regardless of HBeAg status or age.
(Strong recommendation, low quality of evidence)

Who not to treat but continue to monitor:
Where HBV DNA testing is not available: Treatment can be deferred in HBeAg-positive persons aged
30 years or less and persistently normal ALT levels.

(Conditional recommendation, low quality of evidence)

Who not to treat but continue to monitor: Continued monitoring is necessary in all persons with CHB, but in particular those who do not currently meet the above-recommended criteria for who to treat or not to treat, to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease. These include:

- persons without cirrhosis aged 30 years or less, with HBV DNA levels >20 000 IU/mL but persistently normal ALT levels;
- HBeAg-negative persons without cirrhosis aged 30 years or less, with HBV DNA levels that fluctuate between 2000 and 20 000 IU/mL, or who have intermittently abnormal ALT levels;
- Where HBV DNA testing is not available: Persons without cirrhosis aged 30 years or less, with persistently normal ALT levels, regardless of HBeAg status.

Who not to treat but continue to monitor: It is recommended that the following be monitored at least annually:

(Strong recommendation, moderate quality of evidence)

- ALT level (and AST for APRI), HBsAg, HBeAg, and HBV DNA levels (where HBV DNA testing is available)
- Non-invasive tests (APRI score or FibroScan) to assess for the presence of cirrhosis, in those without cirrhosis at baseline;
- If on treatment, adherence should be monitored regularly and at each visit.

More frequent monitoring: In persons who do not yet meet the criteria for antiviral therapy: More frequent monitoring for disease progression may be indicated in: persons who have intermittently abnormal ALT levels or HBV DNA levels that fluctuate between 2000 IU/mL and 20 000 IU/mL (where HBV DNA testing is available), and in HIV-coinfected persons.

(Conditional recommendation, low quality of evidence)

More frequent monitoring: In persons on treatment or following treatment discontinuation: More frequent on-treatment monitoring (at least every 3 months for the first year) is indicated in: persons with more advanced disease (compensated or decompensated cirrhosis); during the first year of treatment to assess treatment response and adherence; where treatment adherence is a concern; in HIV-coinfected persons; and in persons after discontinuation of treatment.

(Conditional recommendation, very low quality of evidence)
Monitoring for tenofovir and entecavir toxicity: Measurement of baseline renal function and assessment of baseline risk for renal dysfunction should be considered in all persons prior to initiation of antiviral therapy.

Monitoring for tenofovir and entecavir toxicity: Renal function should be monitored annually in persons on long-term tenofovir or entecavir therapy, and growth monitored carefully in children. (Conditional recommendation, very low quality of evidence)

Monitoring for hepatocellular carcinoma: Routine surveillance for HCC with abdominal ultrasound and alpha-fetoprotein testing every six months is recommended for:

- persons with cirrhosis, regardless of age or other risk factors (Strong recommendation, low quality of evidence)
- persons with a family history of HCC (Strong recommendation, low quality of evidence)
- persons aged over 40 years (lower age may apply according to regional incidence of HCC), without clinical evidence of cirrhosis (or based on APRI score ≤2), and with HBV DNA level >2000 IU/mL (where HBV DNA testing is available). (Conditional recommendation, low quality of evidence)

Source: WHO, Guidelines for the screening, care and treatment of persons with chronic hepatitis B infection. 2015