FEDERAL MINISTRY OF HEALTH
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ABUJA, NIGERIA

RAPID ADVICE:

UPDATES TO THE NATIONAL GUIDELINES FOR THE PREVENTION, TREATMENT, AND CARE OF VIRAL HEPATITIS IN NIGERIA

National, AIDS, Viral Hepatitis, and STIs Control Programme.

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National AIDS and STIs Control Programme
Federal Ministry of Health and Social Welfare,
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FOREWORD

Nigeria contributes significantly to the burden of chronic viral hepatitis infection globally with a prevalence of 8.1% and 1.1% for viral hepatitis B and C respectively according to the 2018 National HIV/AIDS Indicator and Impact Survey. This corresponds to above 20 million people living with viral hepatitis B and/or C in a population of over 117 million individuals, who are not aware and are at the risk of developing chronic complications of liver cirrhosis and primary liver cell cancers. The most worrisome is the continuous spread of the infections due to high-risk sexual and injection practices in the communities.

Following the expiration of the first edition of the first edition of the National Guidelines for the Prevention, Treatment and Care of Viral Hepatitis in Nigeria in 2020, and in response to the World Health Assembly resolution for member nations to take action in the prevention, diagnosis, and treatment of viral hepatitis, the Federal Government of Nigeria embarked on this noble effect of revising the guidelines.

The revised National Guidelines for the Prevention, Treatment and Care of Viral Hepatitis was developed with the guiding principle of putting people at the center of the response; addressing unique priorities for each population group and geographical area; taking a shared approach towards strengthening health and community systems and responding to a swiftly changing health and development context. The review also considered changes in health system post COVID-19 pandemic.

This protocol provides guidance on treatment approaches and interventions on mother to child transmission of viral hepatitis, reaching children, adolescents, and adult, and high-risk populations with viral hepatitis B vaccination; ensuring safety of blood transfusion services, organ donation and injection practices as well as use of new antiviral drugs for the treatment and cure of viral hepatitis B and C respectively. A simplified approach to providing diagnosis and treatment for persons infected with viral hepatitis B and C was also captured in these guidelines as well as a minimum package for different levels of health care delivery in Nigeria.

It is expected that strict adherence to these guidelines will assist with providing quality and efficient management of hepatitis B and C among infected children, adolescents and adults, as well as contribute significantly to achieving a reduction in the burden and impact of the disease in Nigeria, which are major ingredients toward reaching global elimination by 2030. I, therefore encourage all healthcare providers to avail themselves with a copy of these guidelines in order to update their knowledge and skills for the purpose of providing appropriate care at service delivery points.

Prof. Muhammad Ali Pate.
Coordinating Minister of Health and Social Welfare

ACKNOWLEDGEMENTS

On behalf of the Federal Ministry of Health, I wish to commend and appreciate the stakeholders and donor agencies who immensely contributed to the development of this document. This process would not have been successful without your technical guidance and financial support which have made the production of this document possible.

I would like to express our sincere gratitude to the members of the National Technical Working Group for the Control of Viral Hepatitis, including World Health Organization (WHO), Clinton Health Access Initiative (CHAI), representatives from the Society for Gastroenterologists and Hepatologists of Nigeria (SOGHIN), Association of Public Health Physicians of Nigeria (APHPN) and the academia for their technical expertise and immense contributions and inputs. Our appreciation also extends to US Centres for Disease Control and Prevention (CDC), John Hopkins Programme for International Education in Gynaecology and Obstetrics (JHPIEGO), United Nations Office on Drugs and Crime (UNODC), Yakubu Gowon Centre (YGC), Abbott Laboratories and Civil Society Organisations (CSOs) for their relentless efforts in the development of the new guidelines on Viral Hepatitis Prevention, Treatment and Control in Nigeria.

We are highly grateful for the financial support from Abbott Laboratories, CHAI and WHO during the process of developing this document. Also, we appreciate our colleagues from the Department of Hospital Services, National Blood Service Commission (NBSC) and National Primary Health Development Agency (NPHCDA) for their involvement and sharing their experiences while developing this protocol.

Finally, we thank the staff of the National AIDS, Viral Hepatitis and STIs Control Programme (NASCP) for their perseverance and team spirit in coordinating the development of these guidelines and ensuring that the Federal Ministry of Health through NASCP delivers on its mandate in formulating policies and guidelines on the Viral Hepatitis Control Programme.

Dr. Chukwuma Anyaike
Director and Head, Department of Public Health

EXECUTIVE SUMMARY

This rapid advice provides updated, evidence-informed recommendations on key priority topics around the management of HBV. These include expanded and simplified treatment criteria for adults but now also for adolescents; expanded eligibility for antiviral prophylaxis for pregnant women to prevent mother-to-child transmission of HBV; and improving HBV diagnostics using point-of-care HBV DNA viral load and reflex approaches to HBV DNA testing; and who to test and how to test for HDV infection.

The recommendations are:
Expanded treatment eligibility and antiviral prophylaxis

- Use of non-invasive tests for staging of liver disease.
- Who to treat among people with CHB.
- First-line antiviral therapies for CHB.
- Preventing mother-to-child transmission of hepatitis B using antiviral prophylaxis.
- Treatment of adolescents and children with CHB.

Hepatitis B DNA and HDV infection diagnostics

- Measurement of HBV DNA to guide treatment eligibility and monitor response.
- HBV DNA reflex testing.
- HDV testing - who to test and how to test, including reflex testing for hepatitis delta coinfection.

HBV Service Delivery

- Eight approaches to promote access and delivery of high-quality health services for CHB

Dr Adebobola Bashorun,
Director, Federal Ministry of Health
National Coordinator, National AIDS, Viral Hepatitis and STI Control Programme

ABBREVIATIONS

ALT	Alanine aminotransferase
ART	Antiretroviral therapy
ARV	Antiretroviral
AST	Aspartate aminotransferase
Anti-HBc	Hepatitis B core antibody
Anti-HBe	Antibody to hepatitis B e antigen
Anti-HBs	Antibody to hepatitis B surface antigen
CHB	Chronic hepatitis B
CHD	Chronic hepatitis D
CrCl	Creatinine clearance
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
GFR	Glomerular filtration rate
HBcAg	Hepatitis B core antigen
HBcrAg	Hepatitis B core-related antigen
HBeAg	Hepatitis B e antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis D (delta) virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
PCR	Polymerase chain reaction
PEPFAR	United States President's Emergency Plan for AIDS Relief
POC	Point of Care

CONTENTS

1.0 Background

Nigeria developed her 2023 national guidelines for the prevention, treatment, and care of viral hepatitis in line with the recommendations of the 2021 WHO guidelines on preventing mother-to-child transmission of HBV using antiviral prophylaxis in pregnancy and the WHO Global Progress Report on HIV, Viral Hepatitis, and Sexually Transmitted Infections (STIs).

1.1 Rationale for Development of Rapid Advice

The WHO 2024 HBV guidelines prescribe new recommendations generated from systematic reviews, modelling and cost-effective analyses, and acceptability, values and preferences surveys in collaboration with key stakeholders towards simplifying the HBV management pathway and improving access to care especially in resource-limited settings. These updated recommendations cut across treatment eligibility, HBV testing and PMTCT.

This National Rapid Advice is to provide updates to the 2023 National guidelines for the prevention, treatment, and care of viral hepatitis. These include expanded and simplified treatment criteria for adults and adolescents, expanded eligibility for antiviral prophylaxis for pregnant women to prevent mother-to-child transmission of HBV, use of point-of-care HBV DNA viral load and reflex approaches to HBV DNA testing, and who to test and how to test for HDV infection.

Some of the evidence to support the updated recommendations are highlighted below:

- **Expanded Treatment Eligibility and Antiviral Prophylaxis:** Evidence of missed opportunities arising from the high APRI score cut-off of >2 led to revised recommendations focusing on diagnosing at lower fibrosis stages and providing treatment to prevent progression to further complications. The updated recommendations for expanded and simplified treatment eligibility prioritize capturing larger proportions of HBsAg-positive people based on access to HBV DNA as well as revised HBV DNA thresholds to maximize the benefits of antiviral therapy. Additionally, expanded eligibility for antiviral prophylaxis in pregnant women was informed by overall access to HBV DNA in various settings as well as modelling estimates highlighting significant positive impact on PMTCT of HBV; with an estimated 4.9 million neonatal infections averted from universal prophylaxis for all HBsAg-positive pregnant women.
- **Hepatitis B DNA and HDV Infection Diagnostics:** Recommendations for the use of alternative diagnostic platforms such as POC devices for HBV DNA testing were based on limited access to laboratory-based HBV DNA NAT assays in low-income/resource-limited settings and increased availability of POC platforms for HIV, TB and COVID-19 care. This

takes into consideration evidence of high diagnostic accuracy of POC devices for HBV in comparison to laboratory-based assays, as well as evidence suggesting increased HBV DNA testing uptake and reduced turnaround time to treatment initiation. In addition, laboratory and/or clinic-based reflex testing was recommended to improve access to and uptake of HBV viral load testing.

- **Monitoring and Second-line Therapies:** Recommendations for monitoring of people receiving and not receiving treatment remain focused on evaluating effectiveness of treatment response, adherence and adverse events. Evidence from the 2015 guidelines remain relevant and inform maintained recommendations on monitoring approaches and frequency during treatment.
- **Viral Hepatitis Service Delivery:** This includes innovative strategies to promote uptake of testing services and linkage to care, adherence and retention in care, and integration among others.

1.2 What will this Rapid Advice Address?

This Rapid Advice document will provide updates to the national guidelines and recommendations for the management of chronic HBV infection in Nigeria. It aims to enhance the current understanding and application of treatment protocols among healthcare providers, policymakers and program managers. The advice contained herein is based on the latest evidence and aligns with global best practices, ensuring that the management of HBV in Nigeria is both effective and sustainable. The key areas addressed by this Rapid Advice are as follows:

1.2.1 Expanded Treatment Eligibility and Antiviral Prophylaxis

- **Use of Non-invasive Tests:** Implementation of non-invasive tests for accurately staging liver fibrosis which will help in the decision-making process for treatment initiation.
- **Criteria for Treatment:** Clear guidelines on who should receive treatment among individuals with CHB, ensuring that those who need it most are prioritized.
- **First-line Antiviral Therapies:** Recommendations on the most effective first-line antiviral therapies for CHB focusing on efficacy, safety, and patient tolerance.
- **Preventing Mother-to-Child Transmission:** Strategies for the use of antiviral prophylaxis to prevent mother-to-child transmission of HBV, which is a critical step in reducing the incidence of HBV infection in newborns.

- **Treatment for Adolescents and Children:** Specific guidelines for treating adolescents and children with CHB, which addresses the unique considerations and needs of this population.

1.2.2 Hepatitis B DNA and HDV Infection Diagnostics

- **HBV DNA Measurement:** Protocols for the measurement of HBV DNA to guide treatment eligibility and monitor treatment response, ensuring that patients receive timely and appropriate care.
- **HBV DNA Reflex Testing:** Implementation of reflex testing to improve the accuracy and efficiency of HBV diagnosis and monitoring.
- **HDV Testing:** Guidelines on testing for Hepatitis Delta virus (HDV) coinfection, including who should be tested and the methods to be used, to ensure comprehensive management of HBV.

1.2.3 Monitoring and Second-line Therapies

- **Second-line Antiviral Therapies:** Guidelines on the use of second-line antiviral therapies for managing treatment failure, providing options for patients who do not respond to initial treatments.
- **Monitoring Protocols:** Recommendations for monitoring treatment response and managing side effects, ensuring that patients are continually assessed and supported throughout their treatment journey.
- **Surveillance for Hepatocellular Carcinoma (HCC):** Surveillance strategies for early detection and management of HCC, a potential complication of chronic HBV infection.
- **Therapy Discontinuation and Re-initiation:** Criteria for when to stop and restart antiviral therapy, ensuring that treatment is optimized for each patient's needs and circumstances.

1.2.4 Viral Hepatitis Service Delivery

- Recommendations on approaches to promote access to high quality HBV service delivery consider key learnings from simplified service delivery models for HIV and Hepatitis.
- This includes innovative strategies to promote uptake of testing services and linkage to care, adherence and retention in care, and integration among others.

By addressing these critical areas, this Rapid Advice aims to improve the overall management of chronic Hepatitis B in Nigeria, ensuring that patients receive the best possible care based on the latest evidence and global recommendations.

2.0 Updates to existing guidelines

2.1 Who to treat among people with Chronic Viral Hepatitis B (CHB)

New recommendations

Treatment is recommended for all adults and adolescents (aged ≥12 years) with chronic hepatitis B (CHB)[a] (including pregnant women and girls and women of reproductive age) with:

- Evidence of significant fibrosis (≥F2)[b] based on an APRI score of ***>0.5*** or transient elastography value of ***>7.0*** kPa or evidence of cirrhosis (F4) based on clinical criteria[b] (or an APRI score of >1.0 or transient elastography value of >12.5 kPa)[c], regardless of HBV DNA or ALT levels.

OR

- HBV DNA >2000 IU/mL and an ALT level above the upper limit of normal (ULN) (30 U/L for men and boys and 19 U/L for women and girls). For adolescents, this should be based on ALT>ULN on at least two occasions in a 6- to 12-month period.[d]

OR

- Presence of coinfections (such as HIV, hepatitis D (HDV) or hepatitis C (HCV)); family history of liver cancer or cirrhosis; immune suppression (such as long-term steroid use, solid organ or stem cell transplant); comorbidities (such as diabetes or metabolic dysfunction–associated steatotic liver disease); or extrahepatic manifestations (such as glomerulonephritis or vasculitis), regardless of the APRI score or HBV DNA or ALT levels.

OR

In the absence of access to an HBV DNA assay:

- Persistently abnormal ALT levels alone (defined as two ALT values above the ULN at unspecified intervals during a 6- to 12-month period), regardless of APRI score.[e]

[a] *Defined as the presence of HBsAg on at least one occasion, and for adolescents and children, persistence of HBsAg for six months or more.*

[b] *The thresholds of non-invasive tests (APRI and transient elastography) for diagnosis of significant fibrosis or cirrhosis and treatment recommendation are based on extrapolating data from adults and have not yet been fully validated for adolescents or children.*

[c] *Clinical features of decompensated cirrhosis: portal hypertension (ascites, variceal haemorrhage and hepatic encephalopathy), coagulopathy or liver insufficiency (jaundice). Other clinical features of advanced liver disease and cirrhosis may include hepatomegaly, splenomegaly, pruritus, fatigue, arthralgia, palmar erythema and oedema.*

[d] *The ULN for ALT have been defined as <30 U/L for men and boys and <19 U/L for women and girls for consistency. Some guidelines use different ULN ALT levels for adolescents and children (<22 U/L for girls and women and <25 U/L for boys and men). Raised ALT may normalize in pregnancy and is therefore not a good marker for deciding about long-term treatment in pregnancy. Pregnant women should be reassessed after delivery.*

[e] *Persistently normal or abnormal may be defined as two ALT values below or above the ULN at unspecified intervals during a 6- to 12-month period. ALT levels fluctuate with CHB and require longitudinal monitoring to determine the trend.*

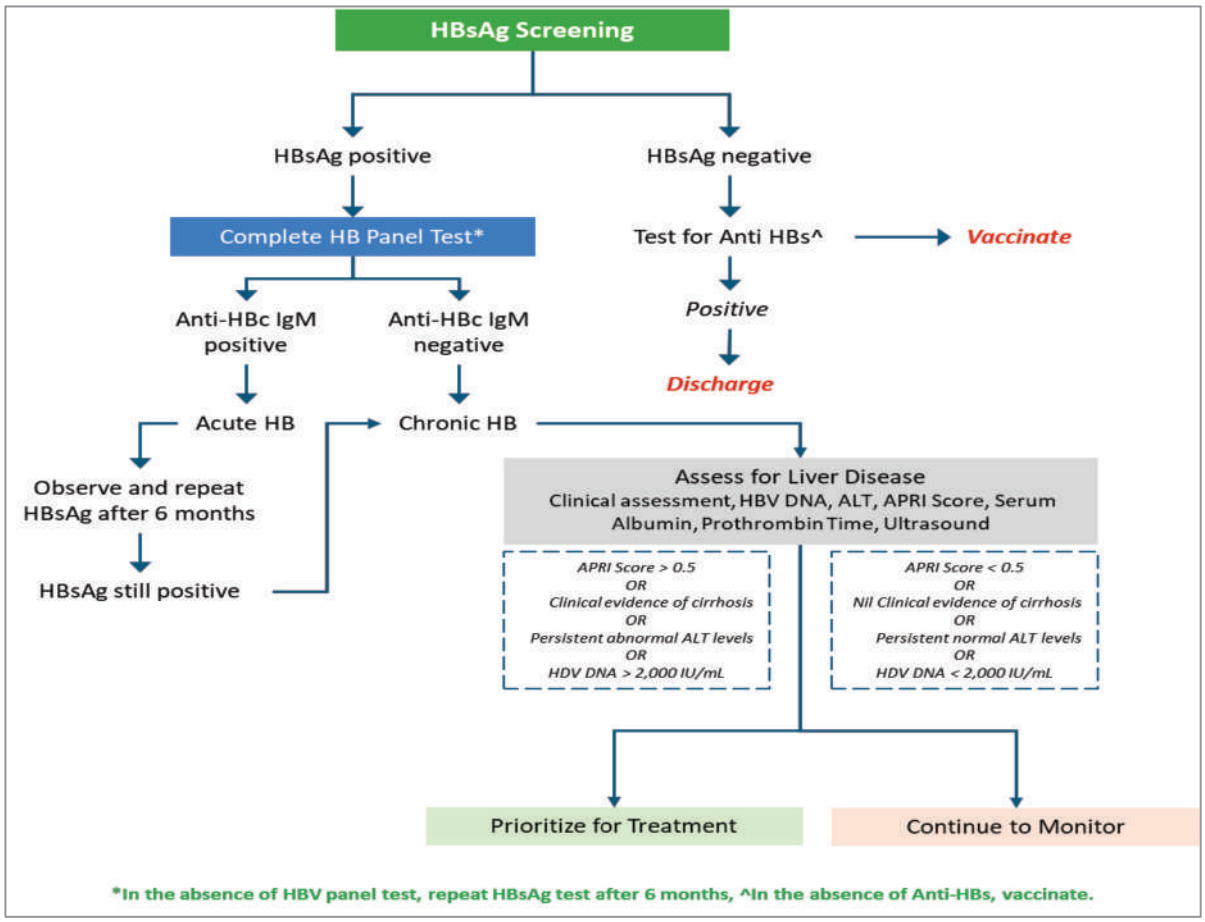

Figure 1: Updated HBV screening algorithm

2.2 First-line antiviral therapies

Entecavir (ETV) or Tenofovir Alafenamide (TAF)[f] (if available) are recommended for people with established osteoporosis and/or impaired kidney function, and for children (ETV for those aged two years or older) or adolescents (TAF for those aged 12 years or older) as alternative regimen), for whom antiviral therapy is indicated.

2.3 Preventing mother-to-child transmission of HBV using antiviral prophylaxis

The 2023 National guidelines for the prevention, treatment, and care of Viral Hepatitis in Nigeria recommends that all HBsAg positive pregnant women be screened with HBV DNA or HBeAg for the prevention of mother to child transmission of HBV and pregnant women with HBV DNA ≥200,000 IU/mL or positive HBeAg[g] should be commenced on Tenofovir Disoproxil Fumarate (TDF)[h] prophylaxis from 28th week of pregnancy.

[f] TAF is not recommended if eGFR is <15mL/min except the patient is on haemodialysis

[g] The use of the HBeAg recommendation represents an additional option for determining eligibility, but HBeAg RDTs have poor diagnostic performance, which limits their routine use in low- and middle-income countries.

[h] TAF may be considered for people (including pregnant women) with impaired kidney function and/or osteoporosis but is not yet approved for hepatitis B treatment in pregnancy (see Chapter 6). TAF is not recommended if eGFR is <15 ml/min except if the patient is on haemodialysis.

This update recommends the following:

2.3.1 **Antiviral prophylaxis among pregnant women and adolescent girls in settings where HBV DNA or HBeAg testing is available**: pregnant women with HBV DNA ≥200,000 IU/mL or positive HBeAg should be commenced on Tenofovir Disoproxil Fumarate (TDF) prophylaxis anytime from the 26th week of pregnancy up until 6 weeks after delivery), to prevent the mother-to-child transmission (MTCT) of HBV.

2.3.2 **Antiviral prophylaxis among pregnant women and adolescent girls in settings where HBV DNA or HBeAg testing is NOT available**: prophylaxis with Tenofovir Disoproxil Fumarate (TDF)b is recommended for all HBV-positive (HBsAg-positive) anytime from the 26th week of pregnancy up until 6 weeks after delivery, to prevent the mother-to-child transmission (MTCT) of HBV.

N:B: *For Babies who have access to HBV birth dose at birth or within 24 hours of birth, maternal prophylaxis can be stopped at birth. Otherwise, maternal prophylaxis should be continued until 6 weeks after birth when at least the birth dose and 1st dose of HBV pentavalent vaccine would have been taken*.

2.3.3 All pregnant women and girls of reproductive age should be assessed first for eligibility for long-term treatment for their own health.

2.3.4 All pregnant women whose antiviral prophylaxis was based on HBsAg testing alone, should be evaluated for eligibility for continued antiviral therapy after delivery.

2.3.5 All interventions should be given in addition to at least three doses of hepatitis B vaccination for all infants, including a timely birth dose.

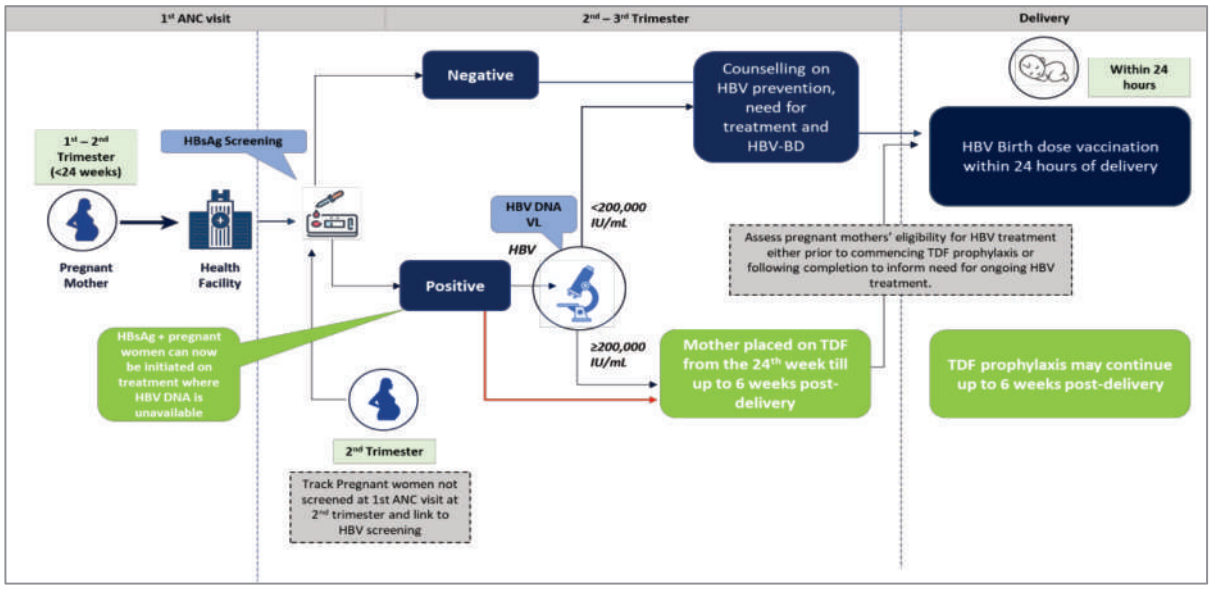

Figure 2: HBV PMTCT Patient Pathway

2.4 HBV DNA Testing

- **Point-of-care (POC) HBV DNA assays:** POC HBV DNA nucleic acid test (NAT) assays may be used as an alternative approach to laboratory-based HBV DNA testing to assess HBV DNA level for treatment eligibility and to monitor treatment response.

  This recommendation for the use of POC HBV DNA assay may only be applicable for patients planned for chemotherapy or steroid use to avoid flaring of HBV infection.

- **Reflex HBV DNA testing:** Where available, Reflex HBV DNA testing for those testing positive on HBsAg may be used as an additional strategy to promote linkage to care and treatment.

  This can be achieved through either laboratory-based reflex HBV DNA testing using a sample already held in the laboratory or clinic-based reflex testing in a health-care facility through immediate sample collection following a positive HBsAg rapid diagnostic test (RDT).

2.5 Hepatitis Delta Virus (HDV) TESTING

Figure 3: Who to test for HDV infection

2.5.1 Who to test for HDV infection

For people with CHB, serological testing for anti-HDV antibodies must be performed for all individuals who are HBsAg positive as the preferred approach to scale up access to HDV diagnosis and linkage to care. In settings in which a universal anti-HDV antibody testing approach is not feasible because laboratory capacity or other resources are limited, testing for anti-HDV may be given priority in specific populations of HBsAg-positive individuals, including the following:

- People born in HDV-endemic countries, regions, and areas.
- People with advanced liver disease, those receiving HBV treatment, and those with features suggesting HDV infection (such as low HBV DNA with high ALT levels); and
- People considered to have increased risk of HDV infection, including haemodialysis recipients, people living with hepatitis C or HIV, people who inject drugs (PWID), sex workers (SW) and men who have sex with men (MSM).

2.5.2 How to test for HDV infection: testing strategy and choice of serological and NAT assays

- People with CHB (HBsAg positive) may be diagnosed with hepatitis D by using a serological assay to detect total anti-HDV followed by an NAT to detect HDV RNA and active (viraemic) infection among those who are anti-HDV positive. Assays should meet minimum quality, safety, and performance standards.[i]

[i] The NAT for detecting HDV RNA should be harmonized with the WHO HDV RNA standard and the results reported in IU/mL. The assays should have a limit of detection of 100 IU/mL or better. Primers used in in-house assays should target the ribozyme region, which is the most conserved region of the HDV genome, for genotype inclusivity.

2.5.3 How to test for HDV infection: laboratory-based reflex testing

- Reflex testing for anti-HDV antibody testing following a positive HBsAg test result and for HDV RNA testing (where available) following a positive anti-HDV antibody test result may be used as an additional strategy to promote diagnosis.

2.5.4 Treatment of HBV/HDV co-infection

- The presence of HBV/HDV coinfection is an indication for treatment of CHB irrespective of other results. Treatment is with TDF or TAF or ETV until the HBV DNA is no longer detectable. In the presence of detectable of HDV RNA, pegylated interferon is the drug of choice provided there is no decompensated liver disease.

2.6 Monitoring for people in care and those receiving treatment

- For people receiving treatment, the following are recommended to be monitored at least annually:
    i. Non-invasive tests (APRI score or transient elastography) to assess stage of disease and progression of fibrosis or cirrhosis; and
    ii. ALT levels (and AST for APRI), HBV DNA levels (when HBV DNA testing is available), HBsAg and HBeAg/anti-HBe.
    iii. Treatment adherence should be monitored regularly and at each visit
    iv. More frequent on-treatment monitoring (every 3-6 months for the first year) may be performed for: people with more advanced disease (compensated or decompensated cirrhosis); during the first year of treatment to assess treatment response and adherence; if treatment adherence is a concern; for people coinfected with HIV; and for people with renal impairment.

- Monitoring for people not yet receiving treatment

  People who do not currently meet the criteria for antiviral therapy (persistently normal serum aminotransferase results and HBV DNA levels below 2000 IU/mL (when HBV DNA testing is available) or who have expressed a desire to defer treatment may be monitored annually for disease progression and ALT and HBV DNA levels (when HBV DNA testing is available).

Note: (In addition to above monitoring, both those on and off treatment should be monitored twice yearly with alpha feto protein and ultrasound scan where possible for the detection or early liver cancer. Both those on treatment and those not suitable for treatment may unfortunately develop liver cancer so it is important to keep this in mind all the times).

2.7 HBV Service Delivery

Eight Approaches to promote access and delivery of high-quality health services for CHB

- Strategies to promote uptake of testing and strengthen linkage to care, treatment and prevention
- Strategies to promote and sustain adherence to long-term antiviral therapy
- Strategies to promote retention in care and track and re-engage those disengaged from care

- Integrating hepatitis testing, care and treatment with other services (such as HIV services and primary care) to increase the efficiency and reach of hepatitis services
- Decentralized testing and treatment services at primary health facilities or HIV and ART clinics to promote access to care
- Task-sharing
- Differentiated care strategy
- Community engagement and peer support

3.0 Next Steps and Conclusion

All National guidelines, training manual, recording, and reporting tools and other relevant policy documents for the prevention, treatment, and care of Viral Hepatitis in Nigeria would be updated to reflect the new recommendations. These recommendations which supersedes all other recommendations made before December 2024 are intended for use by trained healthcare workers in primary, secondary and tertiary health facilities in Nigeria. Accordingly, all 36 states and the Federal Capital Territory Viral Hepatitis Control Programmes and partners should collaborate with the National AIDS, Viral Hepatitis and STI control programme to ensure wide dissemination of this rapid advice and support capacity building of relevant healthcare workers to implement these recommendations.