



**NATIONAL GUIDELINES FOR THE
PREVENTION, CARE AND TREATMENT OF
VIRAL HEPATITIS B & C IN NIGERIA**

**NATIONAL AIDS/STIS CONTROL PROGRAM
FEDERAL MINISTRY OF HEALTH**

2016

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

**NATIONAL AIDS/STIS CONTROL
PROGRAMME, FEDERAL MINISTRY OF
HEALTH**

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FOREWORD

Nigeria contributes significantly to the burden of chronic viral hepatitis infection globally with prevalence of 11% and 2.2% for viral hepatitis B and C respectively. This corresponds to above 20 million people living with viral hepatitis B and/or C in a population of 177 million individuals who are not aware and are at the risk of developing chronic complications of liver cirrhosis and primary liver cell cancers. Most worrisome is the risk of transmitting the infection to other unsuspecting members in the communities.

The National Guidelines for the Prevention, Treatment and Care of Viral Hepatitis in Nigeria has been developed with the guiding principle of achieving Universal coverage through accessible, affordable, available health services based on human rights and equity. Other considerations include government ownership, effective partnership and the use of public health approach for effective and efficient programme implementation.

This document provides strategies towards achieving the global target of eliminating viral hepatitis by 2030 as endorsed by the United Nations member States at the 59th World Health Assembly of 2016 which include protecting against mother to child transmission of viral hepatitis, reaching every child, adolescents, adults and high risk population groups with viral hepatitis B vaccination, ensuring safety of blood transfusion services, organ donation and injection practices and the use of new antiviral drugs for the treatment and cure viral hepatitis B and C respectively.

It is expected that strict adherence to the guidelines will provide the required platform for the attainment of the goal of reducing mortality, morbidity and socio-economic impact of viral hepatitis in Nigeria.

Professor Isaac Folorunso Adewole FAS, FSPSP, DSc (Hons)

Honourable Minister of Health,
Federal Republic of Nigeria



PREFACE

This is the first edition of the National Guidelines for Prevention, Treatment and Care of Viral Hepatitis in Nigeria. It is in response to the World Health Assembly resolution for member nations to take action in the prevention, diagnosis and treatment of viral hepatitis that the Federal Government of Nigeria embarked on this noble project to combat the spread of Viral Hepatitis which has been described as a silent epidemic.

The development of this document spanned rigorous processes. It involved various stakeholders including the Academia, Development Partners, Programme managers, Civil Society Organizations, representatives from the states of the federation, pharmaceutical companies, Funders and the United Nations organizations.

The guidelines have been developed with the guiding principle of achieving Universal coverage through accessibility, affordability, availability and human rights and equity. Other considerations include government ownership, effective partnership and the use of public health approach for effective and efficient programme implementation.

The guidelines provide a framework for health care service delivery in the Prevention, Care and treatment of Viral Hepatitis in Nigeria in line with the global aspiration of eliminating viral hepatitis by 2030 as endorsed by the United Nations member States at the 59th World Health Assembly of 2016.

This document is recommended for use by all stakeholders including policy makers at all levels of government, healthcare workers, civil society organizations, local and international partners.

Dr. (Mrs) Amina M. B. Shamaki mni

Permanent Secretary, Federal Ministry of Health, Nigeria



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We thank our colleagues from the other departments of the Federal Ministry of Health including the National Blood Transmission Centre, Epidemiology Division, National Agency for Food and Drug Administration and Control, National Primary Health Development Agency, National Cancer Control Programme and the Non- Communicable Disease Division of the Department of Public Health.

We thank the staff of the National AIDS and STIs Control Programme (NASCP) for effectively coordinating the development of this document and providing the secretariat for the Viral Hepatitis Control Programme in Nigeria.

Dr. Evelyn Ngige

Director Public Health

Federal Ministry of Health, Nigeria



LIST OF CONTRIBUTORS

FMOH

Dr. (Mrs) M. B. Amina Shamaki mni	Permanent Secretary, FMOH
Dr. Evelyn Ngige	Director Public Health, FMOH
Dr. Sunday Aboje	National Coordinator, NASCP, FMOH
Mr. Segilola Araoye	Director PDA, NASCP, FMOH
Dr. Oluwa Oyemakinde	Director DPRS, FMOH
Pharm. Yekeen Oloyede	Director Logistics, NASCP, FMOH
Dr. Anyaike Chukwuma	Consultant Special Grade II/ Head Prevention NASCP, FMOH
Dr. Bridget Okoeguale	Former Director Public Health, FMOH
Mr. Jide Banjo	Assistant Director Lab NASCP, FMOH
Mrs. Francisca Okafor	Assistant Director IPC NASCP, FMOH
Dr. Deborah Odoh	Assistant Director PMTCT NASCP
Mrs. Ima John-Dada	Assistant Director HCT NASCP
O.A. Ombugadu	Assistant Director TCS NASCP
Mr. Emmanuel Abatta	Assistant Director/Head SI NASCP
Dr. B. S. Jibrin	HCU/DPH
Anthonia Ajudua	NCDC
Durojaye Adebayo	NCDC
Alice R. Gyang	NCCP
Mrs Leticia Nwafor	ACSM NASCP
Dr. Olugbenga Ijaodola	Senior Medical Officer/ Prevention NASCP
Dr. Omede Ogu	Senior Medical Officer /Viral Hepatitis NASCP
Emmanuel Audu	CNO
Pharm. Atu Uzoma	Logistics NASCP
Dr. Uba Sabo	Senior Medical Officer, NASCP
Mr. Audu Saliff	Snr Comm Officer, NASCP
Cordelia Ofaka	PMLS NASCP
Mr. Olugbenga Akinbiyi	ACEO/NASCP
Dr. Chamberline Ozigbu	Medical Officer PMTCT, NASCP
Dr. Michael Kingsley	Medical Officer Prevention, NASCP
Dr. Cheshi Fatima	MO NCCP
Bernard O. Bene	MO NCD
Miss. Edwina Bosah	SO Viral Hepatitis, NASCP
Owolabi Kemi	SO
Toro Halima	SMLT
Mrs. Hauwa Maigari	Snr Comm Health Tech, NASCP
Mrs Ima Inyang	CSA, NASCP
Mayaki Lami	ACDO SI NASCP



ACADEMIA

Prof. Olusegun Ojo	SOGHIN
Prof. BSC Uzochukwu	Professor of Public Health, Health Policy & Systems Consultant Community Health Physician
Prof. Dennis Ndububa	SOGHIN
Prof A. O. Malu	BSU Makurdi
Prof. Jesse Otegbayo	SOGHIN
Dr. Funmi Lesi	SOGHIN
Dr. Uhunmwagho	SOGHIN
Dr. Ijoma Uchenna	SOGHIN UNTH Enugu
Dr. Mohammed Borodo	President SOGHIN/AKTH Kano
Dr. Onwuliri D. Chinemerem	Public Health Physician UNTH

SMOH

Dr. Golden Owhonda	Rivers
Michael Oguntoye	Kwara
Dr. Ismail Abdusalam	Lagos
Dr. Okafor Christopher	Enugu
Aliyu Musa	Kaduna
Dr. Oyenuga Olajumoke	Lagos

NAFDAC

Dr. Nabila Dalhatu	Principal Regulatory Officer
--------------------	------------------------------

NPHCDA

Dr. A. D. Dawud	SMO1
Chris Elemeuwa	

NBTS

Kingsley Odiabara	DD Lab
Dr. A. O. Itodo	CMO

NIMR

Rosemary Audu	Virologist
---------------	------------



PARTNERS/CIVIL SOCIETY

Dr. Rex Mpazanje	WHO
Dr. Chidozie Meribe	CDC
Dr. Funke Ilesanmi	WHO
Dr. Ademola Osigbesan	CHAI
Dr. Ena Oru	CHAI
Dr. Justus Jiboye	CHAI
Ben Karmack	CHAI
Folu Lufadeju	CHAI
Dr. Hameed Oladipupo	ROCHE
Dr. Chukwudi Ehibundu	ROCHE
Dr. Adeyemi Doro	Mylan Pharmaceuticals
Mr. David Nwedu	YGC
Dr. Ngozi Mbanugo	YGC/Programme Director
Ismaila Abdulkareem	YGC/Procurement Manager
Hammadyu Yohanna	YGC/Head Internal Control
Ms. Ijeoma Nnaji	NC, Association for the Eradication of Hepatitis
Ibe Chinwe	Association for the Eradication of Hepatitis
Dr. Ekong Ernest	IHVN
Teclair Ndomb	IHVN
Dr. Segun Oyedeji	SFH
Clifford Eze	SFH/PO
Dr. Onyeka E. Uchenna	APIN/Care and Treatment
Olubunmi Amoo	APIN/Prevention Advisor
Itodo E. Sunday	President HAJO NCDPI
Kemi Adekunle	CDI/PO
Alan Benard	CDI/SRO
Dr. Ugo Udu	ED/ACOMS
Ezeomah Emenike	ACOUNS Nig Ltd/Manager
Danjuma K. Adda	WHA African Reg. CCT, Taraba
Dr. Ebiti Williams	CIND/ Kaduna
Aniekwe Perpetua	YAP
Dr. Okezie Onyedinachi	ECEWS
Dr. Charles Onyebuchi	ECEWS



EXECUTIVE SUMMARY

Viral hepatitis is inflammation of the liver caused by one or more of five main hepatic viruses: A, B, C, D and E. Although, these viruses display similar symptoms and the potential to cause liver disease to varying degrees; they however differ significantly in regards to epidemiology, prevention, diagnosis, and care and treatment. Viral hepatitis is a major global health problem with more than 400 million patients chronically infected, causing over 1.4 million deaths per year. Nigeria is among the countries with a high burden of viral hepatitis with a Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) prevalence of 11% and 2.2%, respectively (FMOH 2013).

Knowledge of viral hepatitis remains low among Nigerians despite being a leading infectious cause of death each year. As a consequence, most of the estimated 20 million Nigerians living with viral hepatitis B or C are undiagnosed, increasing the likelihood of future transmission to others and placing them at greater risk for severe, even fatal health complications such as liver cirrhosis and liver cancer (hepatocellular carcinoma).

Some key subpopulations, such as men who have sex with men (MSM) and people who inject drugs (PWID) have a high risk of viral hepatitis infection. Persons living with HIV are also disproportionately affected by viral hepatitis and related adverse health conditions, considering that HIV, HBV, and HCV share common modes of transmission.³ The progression of viral hepatitis is accelerated among persons with HIV; therefore, HIV co-infected persons experience greater liver-related health problems than non-HIV infected persons. Recipients of organs, blood, and tissue, along with persons working or receiving care in health settings continue to be at risk for viral hepatitis infection as well.

Nigeria is among countries with the highest burden of viral hepatitis with the prevalence of HBV and HCV at 11% and 2.2%, respectively. The distribution of HBV by sex is 62.6% of males and 37.4% of females, while the distribution of HCV by sex is 52.4% to 47.6%. Infections are most common among 21-40 year olds, although substantial perinatal and childhood transmissions do occur. Medical personnel, especially surgeons and dentists are at the greatest risk of infection, while other healthcare workers, commercial sex workers, and drivers are also at significant risk of infection. In Nigeria, HBV transmission results in substantial morbidity and mortality from chronic HBV, liver cirrhosis, and hepatocellular carcinoma. Risk factors for transmission in Nigeria include sexual intercourse, local circumcision, local uvelectomy, scarification, tribal marks, surgical procedures, body piercing, home birth, and receipt of blood transfusions

These are the first edition of the Federal Ministry of Health guidelines for the prevention, care and treatment of viral hepatitis especially B and C in Nigeria. These guidelines have been developed for use by policy makers, programme managers, and health-care providers at all levels of care in Nigeria.

The development of this document is aligned with the global principle of eliminating viral hepatitis by 2030 which is in keeping with the United Nations adoption during the 59th World Health Assembly in May 2016. The strategies and recommendations have been adopted based on the principle of achieving universal health coverage including accessibility, availability, affordability



and human rights and equity. Other considerations include government ownership, effective partnership and the use of public health approach.

The recommendations are structured along the continuum of care for persons with chronic viral hepatitis B and C from initial assessment of stage of disease and eligibility for treatment, to initiation of first-line antiviral therapy and monitoring for disease progression, toxicity and hepatocellular cell carcinoma and switch to second-line drugs in persons with treatment failure especially in viral hepatitis B and for viral hepatitis C using antiviral drugs. They are intended for use across age groups and adult populations.

These guidelines are covered in seven (7) chapters. Chapter 2 dealt with the management of viral hepatitis B including prevention of perinatal and early childhood HBV infection through infant hepatitis B vaccination; catch-up vaccination and other prevention strategies in key affected populations such as persons who inject drugs, men who have sex with men, and sex workers; as well as prevention of HBV transmission in health-care settings. The use of alcohol reduction interventions to reduce progression of liver disease in those with CHB was also highlighted. It also recommended the use of simple, non-invasive diagnostic tests to assess the stage of liver disease and eligibility for treatment; prioritize treatment for those with most advanced liver disease and at greatest risk of mortality; and recommend the preferred use of nucleos(t)ide analogues with a high barrier to drug resistance (tenofovir and entecavir, and entecavir in children aged 2–11 years) for first- and second-line treatment. These guidelines also recommend lifelong treatment in those with cirrhosis; and regular monitoring for disease progression, toxicity of drugs and early detection of Hepatocellular cancer. An additional chapter highlights management considerations for specific populations, including those co-infected with HIV, HCV and hepatitis D virus (HDV); children and adolescents; and pregnant women.

.Chapter 3 dwelt on the management of viral hepatitis C, The majority (80%) of HCV infections progresses to Chronic Liver Disease (CLD). Outcomes vary widely from subclinical infection to end stage liver diseases (ESLD, 20%) and liver cancer (5%). It provides the guidelines for screening, treatment and care persons with chronic hepatitis c virus (HCV) infection. The Direct Acting Antiviral Drugs and interferon based regimen are the drugs of choice in the treatment of viral hepatitis C. The treatment regimens and duration depend majorly on the presence of liver cirrhosis in the patient, the viral genotype

Chapter 7 recommended strategies for effective programme management of viral hepatitis including health system strengthening, decentralization of services, task shifting, logistics management, monitoring and evaluation and operational research for the control of viral hepatitis in Nigeria.



ACRONYMS/ABBREVIATIONS

ADR: Adverse drug reaction
AEs: Adverse events
AEFI: adverse events following immunization
AHB: Acute hepatitis B
ALP: Alkaline Phosphatase
ALT: Alanine Transaminase
APRI: AST to platelet ratio index
ART: Anti-Retroviral Therapy
AST: Aspartate Transaminase
CLD: Chronic Liver Disease
Cr: Creatinine
CSOs: Civil Society Organisations
DAAs: Direct-Acting Antivirals
DNA: Deoxyribonucleic Acid
EASL: European Association for the Study of the Liver
EIA: Enzyme immunoassay
ELISA: Enzyme-linked Immunosorbent Assay
EVR: Early Virological Response
FDA: Food and Drug Administration
FDC: Fixed-Dose Combination
FMOH: Federal Ministry of Health
FSW: Female Sex Workers
GFR: Glomerular Filtration Rate
GI: Gastro-Intestinal
HAI: Histological Activity Index
HBV: Hepatitis B Virus
HCC: Hepatocellular Carcinoma
HCV: Hepatitis C Virus
HCWs: Health Care Workers
HDV: Hepatitis D Virus
HEV: Hepatitis E Virus
HIV: Human Immunodeficiency Virus
ICSR: Individual Case Safety Report
IDP: Internally Displaced Persons
IM: Intra-Muscular
INR: international Normalized Ratio
LMICs: Low and Middle-Income Countries
MAH: Marketing Authorization Holder
MSM: Men who have Sex with Men
MTCT: Mother To Child Transmission



NA: Nucleot(s)ide Analogue

NAT: Nucleic Acid Test

NAFDAC: National Agency for Food and Drug Administration and Control

NGOs: Non-Governmental Organizations

NPC: National Pharmacovigilance Centre

NPHCDA: National Primary Health Care Development Agency

PCR: Polymerase Chain Reaction

PHC: Primary Health Care

PMTCT: Prevention of Mother-To-Child Transmission

PRASCO: Pharmacovigilance Rapid Alert System for Consumer Reporting

PT: Prothrombin Time

PV: Pharmacovigilance

PWID: People Who Inject Drugs

RBV: Ribavirin

RDT: Rapid Diagnostic Test

RNA: Ribo-Nucleic Acid

SEs: Side Effects

SMOH: State Ministry of Health

SOGHIN: Society for Gastroenterology and Hepatology in Nigeria

SPHCDA: National Agency for Food and Drug Administration and Control

STI: Sexually Transmitted Infection

SVR: Sustained Virologic Response

TB: Tuberculosis

TDF: Tenofovir Disoproxil Fumarate

WHO: World Health Organization



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CHAPTER ONE

INTRODUCTION

1.0 OVERVIEW

Viral hepatitis is inflammation of the liver caused by one or more of five main hepatic viruses: A, B, C, D and E. Although, these viruses display similar symptoms and the potential to cause liver disease to varying degrees; they however differ significantly in regards to epidemiology, prevention, diagnosis, and care and treatment. Viral hepatitis is a major global health problem with more than 400 million patients chronically infected, causing over 1.4 million deaths per year. Nigeria is among the countries with a high burden of viral hepatitis with a Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) prevalence of 11% and 2.2%, respectively (FMOH 2013).

Knowledge of viral hepatitis remains low among Nigerians despite being a leading infectious cause of death each year. As a consequence, most of the estimated 20-24 million Nigerians living with viral hepatitis B or C are undiagnosed, increasing the likelihood of future transmission to others and placing them at greater risk for severe, even fatal health complications such as liver cirrhosis and liver cancer (hepatocellular carcinoma).

Some key subpopulations, such as men who have sex with men (MSM) and people who inject drugs (PWID) have a high risk of viral hepatitis infection. Persons living with HIV are also disproportionately affected by viral hepatitis and related adverse health conditions, considering that HIV, HBV, and HCV share common modes of transmission.³ The progression of viral hepatitis is accelerated among persons with HIV; therefore, HIV co-infected persons experience greater liver-related health problems than non-HIV infected persons. Recipients of organs, blood, and tissue, along with persons working or receiving care in health settings continue to be at risk for viral hepatitis infection as well.

1.1 GLOBAL PERSPECTIVES

Current rates of viral hepatitis infection in Nigeria are reflective of the global disease burden involving hundreds of millions of persons. One in every 12 persons worldwide is living with viral hepatitis; approximately 240 million persons are infected with chronic HBV and another 80 million are infected with chronic HCV infection. Globally, an estimated 7% of primary liver cancer and 54% of liver cirrhosis cases are caused by viral hepatitis, and approximately 1.4 million deaths from viral hepatitis occur each year.

The proportion of persons living with viral hepatitis is greatest in Asia, sub-Saharan Africa, and Egypt. Nigeria accounts for 8.3% and 4.5% of the global burden of chronic HBV and HCV respectively. The prevalence of HCV infection is particularly high among subpopulations (e.g. people who inject drugs (PWID) and persons living in correctional settings) in many parts of the world.



1.2 EPIDEMIOLOGY

1.2.1 Epidemiology of Viral Hepatitis in Nigeria

Nigeria is among countries with the highest burden of viral hepatitis with the prevalence of HBV and HCV at 11% and 2.2%, respectively. The distribution of HBV by sex is 62.6% of males and 37.4% of females, while the distribution of HCV by sex is 52.4% to 47.6%. Infections are most common among 21-40 year olds, although substantial perinatal and childhood transmissions do occur. Medical personnel, especially surgeons and dentists are at the greatest risk of infection, while other healthcare workers, commercial sex workers, and drivers are also at significant risk of infection. In Nigeria, HBV transmission results in substantial morbidity and mortality from chronic HBV, liver cirrhosis, and hepatocellular carcinoma. Risk factors for transmission specific to Nigeria include local circumcision, local uvelectomy, scarification, tribal marks, surgical procedures, body piercing, home birth, and receipt of blood transfusions.

1.2.2 Viral Hepatitis subtypes

Viral Hepatitis has five major types- A, B, C, D and E, with varying degrees of epidemiology, prevention, diagnosis and treatment.

Hepatitis A Virus (HAV), which is primarily spread via faecal-oral transmission, causes Hepatitis A infection; when an uninfected, unvaccinated person ingests food or water that is contaminated with the faeces of an infected person. The disease is closely associated with unsafe water, inadequate sanitation, and poor personal hygiene. Symptomatic progression is rare with mostly mild cases characterized by full recovery and lasting immunity from further HAV infections. However, a few cases can be severe and life threatening. Safe and effective vaccines are available to prevent HAV infection.

Children are likely to have experienced an episode of hepatitis A virus infection before the age of 10. Those infected in childhood do not experience noticeable symptoms. Epidemics are uncommon due to herd immunity from prior infection. HAV may lead to significant economic and social consequences due to delayed recovery lasting weeks to months; preventing the expedited return to work, school or daily life. The impact on food establishments, with identified HAV as a source of transmission in outbreaks, can be substantial.

HAV rarely causes death. Unlike HBV and HCV, HAV does not cause chronic liver disease and is rarely fatal; however, the infection may cause debilitating symptoms and fulminant hepatitis (acute liver failure), resulting in substantial mortality. Persons with pre-existing chronic liver disease, including chronic HBV and HCV, are at increased risk of serious complications from HAV infection.

Hepatitis B infection is a vaccine-preventable disease transmitted through infected blood, semen, and other body fluids. HBV is 50-100 times more infectious than HIV with several modes of transmission; such as perinatal transmission from infected mother to child, unsafe sexual intercourse, transfusion of HBV-infected blood and blood products, unsafe medical procedures, sharing of needles and sharps and horizontally between children, as well as other intra-familial sources of infection. Globally, it is estimated that 2 billion people have been infected with HBV of which approximately 240 million are chronically infected with HBV. Among those with chronic HBV, up to 30% go on to develop liver disease. The average prevalence rate for HBV in Nigeria



ranges between 11- 13.7% with an estimated 20 million Nigerians chronically infected.” There is no known virologic cure for HBV infection, however antiviral treatment has been shown to reduce the transmission risk, decrease the likelihood of developing liver complications resulting in death and improve prognosis.

Hepatitis C infection is a blood borne virus 10 times more infectious than HIV with no currently available vaccine. The most common modes of transmission are through HCV-infected blood, unsafe medical procedures, and sharing of needles and sharps. Less common modes of transmission are sexual and perinatal transmission. Globally, an estimated 80 million patients are chronically infected resulting in roughly 700 thousand deaths per year. An estimated 3.6 million patients are infected with HCV in Nigeria; however, the epidemiology of HCV in Nigeria is not well defined due to paucity of data. With current HCV direct acting antiviral (DAAs) agents, higher rates of sustained virologic response (SVR) have been recorded globally.

Hepatitis D infection occurs exclusively in persons infected with HBV; replication occurs solely in the presence of HBV. Co-infection with HDV and HBV can result in significant morbidity and mortality. HBV vaccination is protective against both HBV and HDV infections in HBsAg negative individuals.

Hepatitis E infection is transmitted mainly through contaminated drinking water and food. Other transmission routes have been identified, which include transfusion of infected blood products and perinatal transmission. Hepatitis E Virus (HEV) infection is usually self-limiting and resolves within 4–6 weeks. Occasionally, fulminant HEV develops with acute liver failure, which can lead to death. Globally, HEV outbreaks and sporadic cases occur in resource-limited countries with limited access to essential water, sanitation, hygiene and health services, and may affect large numbers of people. In recent years, outbreaks have occurred in areas of conflict and humanitarian emergencies, such as war zones, and in camps for refugees or internally displaced persons (IDP). An estimated 20 million infections and 3.3 million acute cases occur annually worldwide with an estimated 56,600 deaths. HEV infection is associated with increased morbidity and mortality in pregnant women and new-borns. There is no available treatment capable of altering the course of acute HEV, although HEV vaccination exists, it is not widely available. Prevention is the most effective approach against the disease.

As HEV is usually self-limiting, hospitalization is generally not required. However, hospitalization is required for people with fulminant HEV and should also be considered for symptomatic pregnant women. Maintaining standards for public water supplies, establishing proper waste management systems, and maintaining hygienic practices such as hand washing with safe water, particularly before handling food, can reduce the risk of infection and transmission. Avoiding consumption of water and/or ice of unknown purity, and adhering to safe food practices are also useful.

1.3 GUIDING PRINCIPLES

The development of this document is aligned with the National Policy for the Control of Viral Hepatitis in Nigeria. This is founded upon the following principles;

1. Universal Health Coverage: Ensuring that all Nigerians can utilize effective, preventive, curative, and palliative high-quality health care services for viral hepatitis. This can be achieved through the following;



- **Accessibility:** The provision of various viral hepatitis services at different levels of the health care system.
- **Affordability:** The uptake of viral hepatitis prevention, care and treatment, as well as support services should be at minimal cost.
- **Availability:** The provision of viral hepatitis testing, vaccination, pharmaceutical, laboratory as well as care and treatment services should be available at various points of care throughout the health care system.
- **Human rights and equity:** The treatment of patients in a client-focused manner through which all patients receive the same level of care irrespective of gender, ethnicity or social status.

2. Government ownership: Government at the Federal, State, and Local levels should commit to ensuring the goal of health for all citizens through provision of appropriate interventions for viral hepatitis infection.

3. Partnerships: Ensuring evidence-based interventions, services and policies through inter-sectorial collaboration, service/programme integration and involvement of affected people and communities.

4. Public health approach: Adopt the principles of public health approach to provide a useful framework to guide a response to viral hepatitis. The approach will include definition of the problem through systematic collection of information about the magnitude, scope, characteristics and consequences of viral hepatitis. It also includes the establishment and implementation of interventions based on research and epidemiological evidence, and monitoring the impact as well as cost effectiveness of interventions.



CHAPTER TWO

MANAGEMENT OF HEPATITIS B

2.1 PREVENTION OF HEPATITIS B

2.1.1 Infant and Neonatal Hepatitis B Vaccination

In Nigeria, the current routine immunization schedule for infants includes four doses of HBV vaccine. The first dose is the monovalent HBV vaccine administered within the first 24 hours of life. Subsequent doses of the vaccine are given as a component of the pentavalent vaccine at 6 weeks, 10 weeks, and 14 weeks of age. The Pentavalent vaccine provides coverage for Diphtheria, Pertussis, Tetanus, Hepatitis B and Haemophilus influenza type B.

Recommendation:

This guideline recommends the above schedule as appropriate

Dosage:

Age	HBV Vaccine	Dose	Route
At birth (within 24 hours)	Monovalent	10µg / 0.5 ml	Intramuscular
6 weeks	Pentavalent	0.5 ml	Intramuscular
10 weeks	Pentavalent	0.5 ml	Intramuscular
14 weeks	Pentavalent	0.5 ml	Intramuscular

2.1.2 Prevention of mother-to-child HBV transmission

The currently recommended practice to reduce mother-to-child perinatal transmission or horizontal transmission relies on the administration of HBV vaccine and concurrent administration of hepatitis B immune globulin (HBIG) and also the administration of oral nucleos(t)ide analogues to HBV-infected pregnant mothers in the 3rd trimester (28 weeks upwards) of pregnancy till delivery.

Recommendation:

- All exposed babies (babies born to HBsAg positive mothers) should receive hepatitis B immune globulin (HBIG) intramuscularly in addition to the HBV vaccine. This HBIG must be given within 24 hours of birth with the 1st dose of HBV vaccine. The site of administration for HBV vaccine and HBIG should be different.
- HBV-infected pregnant women with HBeAg positivity should be treated with nucleos(t)ide analogues.



- HBV-infected pregnant women who are HBeAg negative but with high viraemia ($\geq 200,000$ IU/ml) should be treated with nucleos(t)ide analogues.
- Tenofovir, lamivudine, are the recommended drugs to be used from week 28 till delivery.
 - Entecavir* its safety In pregnancy is not known (ref WHO)

2.1.3. Prevention of hepatitis B transmission in older children, adolescents & adults

- In unvaccinated older children (aged from 1 – 11 years) the recommended schedule is as follows:
Monovalent HBV vaccine at 0, 1 and 6 months should be administered (dose – $10\mu\text{g} / 0.5\text{ml}$, IM)
- In previously unvaccinated adolescents and adults the recommended schedule is as follows:
Monovalent HBV vaccine at 0, 1 and 6 months should be administered (dose – $20\mu\text{g} / 1\text{ml}$, IM)

Indication for immunization in these categories:

- All HBsAg negative individuals should be immunized
- However, where anti - HBs test is done and titre is $\geq 10\text{ mIU/mL}$ then vaccination is not required
- Special Populations
 - Persons who do not respond to first series of Hepatitis B vaccine should complete a second 3-dose vaccine series. The second vaccine series should be given on the usual 0, 1 and 6-month schedule.
 - For HIV, haemodialysis and other Immuno-compromised individuals, it is recommended that the dose of vaccine should be doubled (dose $40\mu\text{g} / 2\text{ml}$) and a fourth dose should be added, following the following schedule – 0, 1, 2, and 6 months

2.1.4 General measures to reduce HBV transmission

Individuals who are HBsAg positive should:

- Adopt correct and consistent condom use during sexual intercourse if the partner is not HBV immune or adequately vaccinated.
- Avoid sharing sharps, razors, toothbrushes, or other personal care items;
- Not donate sperm, blood products or organs;
- Follow standard universal precautions with open cuts or bleeding.

2.1.5 HBV vaccination of household and sexual contacts

Household members and sexual partners of persons with chronic HBV are at increased risk of HBV infection and should be vaccinated if they are negative for HBsAg, anti-HBs, and IgG and anti HBc tests are available, vaccination is recommended when results are negative. Dosing schedules depend on the type of vaccine, age at administration, need for rapid immunization, and previous response to HBV vaccination.

Recommendation:

- Household members and Sexual contacts of persons with Chronic HBV should be vaccinated. *The dose and schedule should be as mentioned above in 2.1.3*



2.1.6 Measures to Reduce Disease Progression in Persons with Chronic Hepatitis B

Alcohol reduction

Significant alcohol intake (>20 g/day in women and >30 g/day in men) can accelerate the progression of HBV-related cirrhosis. It is recommended that a history of alcohol consumption should be taken in all persons with HBV infection, followed by the offer of Brief Intervention (Counselling & health education) for persons with moderate-to-high alcohol intake.

2.1.7 Prevention of hepatitis B transmission in health-care settings

The prevention of hepatitis B transmission in healthcare settings includes

- Hand washing including surgical hand preparation, and use of gloves
- Safe handling and disposal of sharps and waste, safe cleaning of equipment
- Screening of donors, donated blood and blood products.
- Improved access to safe blood
- Vaccination of health care workers
- Build capacity of healthcare personnel
- Post-exposure prophylaxis following needle-stick injury/sexual exposure/mucosal or percutaneous (bite) HBV exposure
 - Wounds should be washed with soap and water, and mucous membranes flushed with water
 - The source individual should be screened for HBsAg, HIV and HCV antibody
 - HBsAg, anti-HBs and IgG anti-HBc should be checked in the exposed individual, to assess whether the individual is infected, immune or non-immune to HBV
 - If the source individual is HBsAg-positive or status is unknown, HBIG (0.06 mL/kg or 500 IU) is given intramuscularly and active vaccination commenced (0, 1 and 6 months) if the exposed individual is non-immune. HBIG and vaccine should be given at different injection sites. HBIG is repeated at 1 month if the contact is HBeAg positive, has high HBV DNA levels or if this information is not known. If the exposed individual is a known non-responder to HBV vaccination, then two doses of HBIG should be given 1 month apart.
 - Anti-HBs titres should be measured 1–2 months after vaccination
- Injection safety in health-care settings - Health care workers are required to use auto-disable syringes for intramuscular, intra-dermal and subcutaneous injections and a sufficient supply of quality-assured syringes with matching quantities of safety boxes in health-care settings. Avoidable unsafe practices ultimately lead to large-scale transmission of blood-borne viruses among patients, health-care providers and the community at large.

Unsafe practices include, but are not limited to the following prevalent and high-risk practices:

- Reuse of equipment to administer injections to more than one person, including reintroduction of injection equipment into multi-dose vials
- Recapping of used needles, and unsafe handling of sharps as they lead to accidental needle-stick injuries in health-care workers, which occur while giving an injection or after the injection
- The use of injections for health conditions where oral formulations are available and recommended as the first-line treatment
- Unsafe sharps waste management, putting health-care workers, waste management



workers and the community at large at risk. Unsafe management of sharps waste includes incomplete incineration, disposal in open pits or dumping sites, leaving used injection equipment in hospital laundry, and other practices that fail to secure infected sharps waste.

2.1.8 Prevention of Sexual Transmission of Hepatitis B Among High Risk Populations

High-risk populations include the following

- Female Sex workers (FSW)
- Male sex workers
- People who inject drugs (PWID)
- Sickle cell anaemia patients
- Inmates of prisons and other correction facilities
- Sexual partners and close contacts of HBV-infected individuals
- Men who have sex with men (MSM)
- Kidney disease patients on maintenance haemodialysis
- Other related high-risk behaviour.

Preventive measures include:

- Promotion of correct and consistent condom use
- Targeting and routine screening of high risk population
- Hepatitis B vaccination
- Developing strategies to increase uptake and complete the hepatitis B vaccination schedule
- Offering peer education interventions to reduce the incidence of viral hepatitis
- Integrated action to increase access to medical and social services for vulnerable persons, victims of rape and discrimination.

2.2 DIAGNOSIS OF HBV

Clinical Evaluation

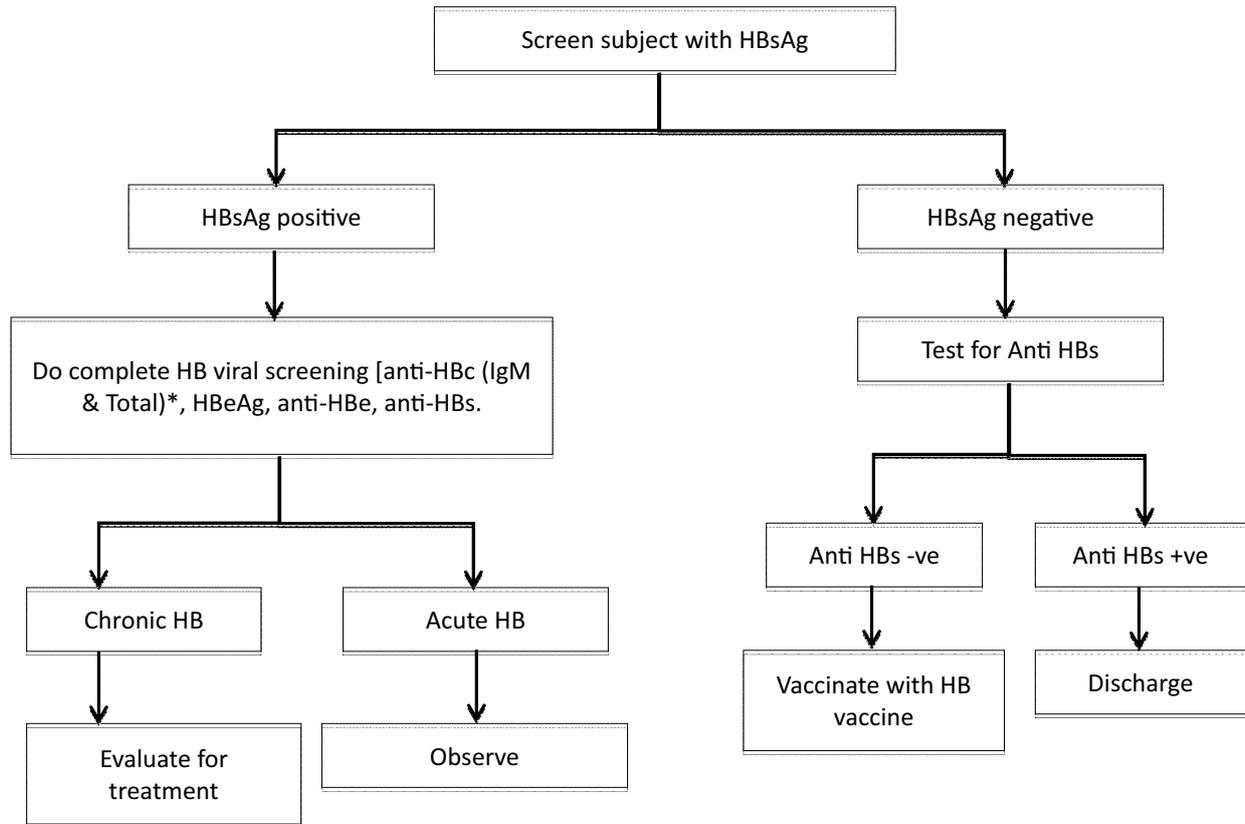
A detailed history and physical examination of patients are required. Alcohol, drugs and history of other risk factors should be taken. Physical examination is conducted to evaluate for features of chronic liver disease such as jaundice, hepatomegaly, splenomegaly and GI bleeding. The presence of ascites is highly suggestive of decompensated liver cirrhosis. These patients should be considered for treatment prioritization and referred for specialized care.

Recommendation:

Following the identification of an HBsAg positive person the following should be done to confirm diagnosis and assess the patient.



SCREENING AND MANAGEMENT OF HEPATITIS B



*In areas where HBV serology panel is inaccessible a repeat HBsAg test is required in 6 months. Where positive, chronic Hepatitis B is confirmed.



Interpretation of Hepatitis B Serologic Tests /Markers

Test	Results	Interpretation
HBsAg	Negative	Susceptible
Anti-HBc	Negative	
Anti-HBs	Negative	
HBsAg	Negative	Immune due to vaccination
Anti-HBc	Negative	
Anti-HBs	Positive with >10mIU/mL*	
HBsAg	Negative	Immune due to vaccination
Anti-HBc	Positive	
Anti-HBs	Positive	
HBsAg	Positive	Acutely Infected
Anti-HBc	Positive	
IgM anti-HBc	Positive	
Anti-HBs	Negative	
HBsAg	Positive	Chronically Infected
Anti-HBc	Positive	
IgM anti-HBc	Negative	
Anti-HBs	Negative	
HBsAg	Negative	Four Interpretations possible
Anti-HBc	Positive	
Anti HBs	Negative	



Interpretation of Hepatitis B Serologic Tests /Markers

Four interpretations:

- 1- May be recovering from acute HBV infection.
- 2- May be distantly immune and the test is not sensitive enough to detect a very low level of anti-HBs in the serum.
- 3- May be susceptible with a false positive anti-HBc.
4. May be chronically infected and have an undetectable level of HBsAg present in the serum (Occult HBV)

Chronic Hepatitis B (CHB) is defined as the persistence of HBsAg for more than 6 months or presence of chronic liver disease attributable to HBV infection. HBeAg: In persons with CHB, a positive HBeAg result usually indicates the presence of active HBV replication and high infectivity. Post vaccination testing, when it is recommended, should be performed 1-2 months following dose #3.

¹⁹ CDC, Epidemiology and Prevention of Vaccine-Preventable Diseases, The Pink Book: Course Textbook - 13th Edition (2015), <http://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html>

Assessment of Liver disease

Assessment of hepatic injury/severity:

Liver injury and the severity can be assessed using the following tests: Aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), bilirubin, albumin, prothrombin time (PT), ultrasonography.

Liver enzymes: Aminotransaminase levels may fluctuate with time, and single measurements of ALT and AST do not indicate disease stage. Usually, the ALT concentrations are higher than those of AST, but with disease progression to cirrhosis, the AST/ALT ratio may be reversed. Tests of liver synthetic function and/or portal hypertension include serum albumin, bilirubin, platelet count and prothrombin time (27,28). A progressive decline in serum albumin concentrations, rise in bilirubin and prolongation of the prothrombin time are characteristically observed as decompensated cirrhosis develops.

Full blood count (including platelet count).

Imaging

Ultrasound scan

CT scan where applicable/necessary

Non-invasive tests (NITs):

Non-invasive methods for assessing the stage of liver disease are supplanting liver biopsy and have been validated in adults with CHB. Blood and serum markers for fibrosis, including APRI and FIB-4, as well as commercial markers such as Fibro Test can be estimated, or transient elastography (Fibro Scan) performed to rule out advanced fibrosis (33–35).

Liver Fibrosis Assessment by Non –Invasive Tests

Aspartate aminotransferase (AST)-to-Platelet Ratio Index (APRI) is a simple index for estimating



hepatic fibrosis based on a formula derived from AST and platelet concentrations. For the purpose of early initiation of patients on therapy, the cutoff of 2.0 should be considered. Below is the formula to be used for APRI Score:

APRI Score and Liver Fibrosis Assessment Formula:

$$\text{APRI} = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelets Count (109)/L}} \times 100$$

NB: In this formula the platelet count is expressed in 1000 of platelets per microliter. If the patient has 137,000 platelets per microliter then you use 137 as the denominator in the formula.

An online calculator can be found at: <http://www.hepatitisc.uw.edu/page/clinical-calculators/apri>

Interpretation of Aminotransferase Platelet Ratio Index (APRI)

<i>APRI Value</i>	<i>Interpretation</i>	<i>Action</i>
<i>>2</i>	<i>High Probability (94%) of F4 Cirrhosis</i>	<i>Prioritize for treatment</i>
<i>Between 1 & 2</i>	<i>Risk of Advanced Fibrosis</i>	<i>Consider for treatment</i>
<i><1</i>	<i>Reduced Risk of Advanced Fibrosis</i>	<i>Consider for treatment</i>
<i><0.5</i>	<i>Less risk of significant Fibrosis</i>	<i>Monitor and/or delay treatment</i>

Liver biopsy:

Liver biopsy has been used to ascertain the degree of necroinflammation and fibrosis, and to help guide the decision to treat. There are several established methods of scoring histology and measuring activity (necroinflammation) separately from staging (fibrosis). However, limitations of biopsy include sampling error, subjectivity in reporting, high costs, the risks of complications, discomfort to the patient, and the need for training and infrastructure in Low middle income countries (LMICs). The pathological features of CHB on liver biopsy depend upon the stage of the disease, host immune response and degree of virus replication.



Liver biopsy findings should be categorized into mild, moderate or severe chronic necroinflammation or, better still, semi- quantitatively scored by a scoring system like the Knodell Histological Activity Index (HAI). Comments about degree of fibrosis should also be included.

Recommendation:

To be done by an appropriately trained physician

2.2.2 Evaluation for Antiviral Therapy in HBV infection

Evaluation for Antiviral Therapy in HBV Infection

HBV Infection: Who to treat.

Recommendation:

- 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. (WHO evidence)
- 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 20 years, and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA $>20,000$ IU/mL), in HBeAg positive patients (APASL, SOGHIN)
- Treatment is recommended for HBeAg negative patients with serum HBV DNA $\geq 2,000$ IU/ml
- Treatment should be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status, in the absence of other known causes of elevated ALT (SOGHIN) HBsAg +ve patient with a Positive family history of liver cancer should be treated irrespective of other parameters.
- HBV Infection: Who not to treat but continue to monitor

Recommendation:

- Antiviral therapy is not recommended and can be deferred in persons without clinical evidence of significant fibrosis (or based on APRI score <2 in adults), or fibroscan evidence where available and with persistently normal ALT level and low levels of HBV replication (HBV DNA <2000 IU/mL), regardless of HBeAg status. (WHO, APASL, EASL)
- Treatment can be deferred in HBeAg- positive persons aged 20 years or less and persistently normal ALT levels. (SOGHIN)
- 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 20 years or less, with HBV DNA levels >2000 IU/mL but persistently normal ALT (SOGHIN)

Goals of Treatment

- a. To achieve undetectable HBV DNA levels
- b. To achieve HBeAg sero-conversion and development of anti-HBe
- c. Normalisation of Serum ALT



- d. To prevent liver disease progression to cirrhosis, liver failure and liver cancer
- e. Loss of HBsAg and development of Anti-HBs
- f. To improve quality of life.

Pre-treatment Counselling

It is important that patients are fully informed in simple terms about the following in order to improve compliance:

2. The health implications of chronic HBV infection (liver failure, Cirrhosis –Hardening /scarring of the liver, Liver cancer)
 - a. The chronic nature of the disease – monitoring and treatment may be lifelong.
 - b. The possibility that spouse(s), children and close relatives may be infected and the need to screen and protect if uninfected.
 - c. The need to avoid further health risks such as alcohol, herbal concoctions, *aflatoxins (mouldy groundnuts)multiple sexual partners, tattooing, scarification marks (to avoid risk of co-infections and possibly re-infection in cases of cure)..
3. The financial implications of treatment options in relation to the desired goal of treatment.
4. Potential side effects of the treatment options should be discussed.

The objectives and likely outcomes of treatment should be discussed in terms of virological response, normalization of liver functions and prevention or reduction in the risk of further liver

HBV Treatment Recommendations

- In all adults, adolescents and children age 12 and above, in whom antiviral therapy is indicated, the nucleos(t)ide analogues (NAs) which have a high barrier to drug resistance (Tenofovir is the preferred drug of choice, or with Entecavir as alternative)are recommended. Entecavir is recommended in children aged 2- 11 years or those who cannot tolerate Tenofovir. (WHO). Tenofovir should be avoided in renal impairment.
- Pegylated interferon therapy is recommended in patients for finite treatment who have following parameters:
Viremia of HBV DNA < 107 IU / ml Elevated serum ALT (> 1x upper limit of normal)

Young patient aged ≤ 45 years(it is approved for use in children aged 2-18years .)

- Pegylated interferon is contraindicated in decompensated cirrhosis

Nas with a high risk of resistance (lamivudine, adefovir & Telbivudine) can lead to drug resistance and are not recommended.

- Telbivudine is preferable in patients with renal impairment,
- Conventional interferon is no longer recommended.

Special Populations

Co–infections

HBV/HCV- Treatment is for the dominant infection while monitoring is for the latent infection, the dominant infection is the infection with the higher viral load.



HBV/HIV- Simultaneous treatment for both diseases; treatment should include drugs effective for both conditions and these include tenofovir+ emtricitabine, in combination with Non-nucleoside reverse transcriptase inhibitor or protease inhibitor.

HBV/HDV- treatment is with Pegylated Interferon for 48 weeks

Chemo/Immunosuppressive therapy

Before commencing chemotherapy, every patient should be screened for HBsAg/anti-HBc as HBV infection may flare on starting treatment. HBsAg positive patients should be started on oral Nucleoside analogues one week before commencement of chemotherapy and continued for 6 months after stopping chemotherapy.

Table 1a. Profile of HBV treatment options

Nucleoside Analogues	RESISTANCE BARRIER	DOSE	DURATION	ROUTE	INDICATION	COST	REMARKS
Tenofovir	Low risk of resistance	300mg dly	Life-long, or until loss of HBsAg/HBeAg positivity	P.O	High viral load	Low	Watch out for Nephrotoxicity
Entecavir	Low risk of resistance	0.5mg dly Lamivudine naïve	Life-long , or until loss of HBsAg/HBeAg positivity	P.O	High viral load	Moderate	Maybe used in place of Tenofovir

Table 1b. Profile of HBV treatment options

Interferons	RESISTANCE BARRIER	DOSE	DURATION	ROUTE	INDICATION	COST	REMARKS
Pegylated Interferon	Not applicable	180mcg wkly	48 weeks	S.C	Low viral load High ALT	high	For finite duration of therapy, Higher HBsAg loss & Higher HBeAg seroconversion



MONITORING AND FOLLOW-UP

Success of therapy is dependent on the proper baseline investigations and monitoring of therapy to determine success and prevent harm to the patient

Baseline investigations to initiate therapy for CHB– in addition to investigations for evaluation include

Serum Electrolyte, Urea and Creatinine for all patients

HIV screening

Exclude non-viral causes of liver disease if suspected (e.g. Liver scan)

Pregnancy test

Psychiatric assessment

HDV test (if available)

Treatment monitoring indices for CHB on Interferon therapy

HBsAg test

White blood cell and Platelet count

HBeAg testing for HBeAg positive patients

HBV DNA

EU,Cr for patients

Serum ALT

Thyroid function test (T3, T4, TSH)

Treatment monitoring indices for CHB on NA Nucleos(t)ide Analogues therapy

HBsAg test

White blood cell and Platelet count

HBeAg testing for HBeAg positive patients

HBV DNA

Serum Creatinine (Cr) for patients

Serum ALT

2.4 MONITORING AND FOLLOW-UP

Success of therapy is dependent on appropriate baseline investigations and patient monitoring for desirable clinical outcomes and reduced risk of harm to the patient.

In addition to investigations for evaluation, the baseline investigation to initiate therapy for CHB includes:

- 1) Serum Electrolyte, Urea and Creatinine for all patients
- 2) HIV screening
- 3) Exclusion of non-viral causes of liver disease if suspected (e.g. Liver scan)



- 4) Pregnancy test
- 5) Psychiatric assessment
- 6) HDV test (if available)

Additionally, treatment monitoring indices for CHB on Interferon therapy

- 1) HBsAg test
- 2) White blood cell and Platelet count
- 3) HBeAg testing for HBeAg positive patients
- 4) HBV DNA
- 5) Electrolytes, Creatinine for patients
- 6) Serum ALT
- 7) Thyroid function tests (T3, T4, TSH)

Treatment monitoring indices for CHB on Nucleos(t)ide Analogues therapy:

- 1) HBsAg test
- 2) HBeAg testing for HBsAg-positive patients
- 3) HBV DNA
- 4) Serum Creatinine (Cr) for patients
- 5) Serum ALT

Table 2. Treatment monitoring for CHB (Nucleos(t)ide analogue Therapy)

BASELINE	4 WEEKS	12 WEEKS	24 WEEKS	48 WEEKS	ANNUALLY	REMARKS
HBV viral load		+			+	Monitor annually subsequently (if available)
ALT	+	+	+			
Serum Creatinine	+	+	+			Monitor annually subsequently
HBsAg test					+	Annual monitoring until HBsAg loss
HBeAg test			+			Annual monitoring

Table 3. Treatment monitoring for CHB (Peg-interferon Therapy)

BASELINE	4 WEEKS	8 WEEKS	12 WEEKS	24 WEEKS	48 WEEKS	18 MONTHS
HBV viral load			+	+	+	+ (End of monitoring for Interferon)
ALT	+	+	+			
Psychiatric assessment						
WBC & Platelet	+	+	+			
Thyroid function				+	+	
HBsAg test				+	+	+

Table 4. Treatment Endpoint/ indices of CHB

AGENTS	DURATION OF TREATMENT	
	HBeAg positive	HBeAg negative
Nucleoside Analogues	6-12 months after HBeAg seroconversion, undetectable serum HBV DNA and appearance of anti HBe	Until HBsAg loss
Pegylated Interferon	48 weeks Sustain Immunological Control HBeAg seroconversion	48 weeks Sustain Immunological Control and Loss of HBs Ag

***Where there are challenges with treatment response refer the patient to the Gastroenterologist/Hepatologist**



CHAPTER THREE

MANAGEMENT OF HEPATITIS C

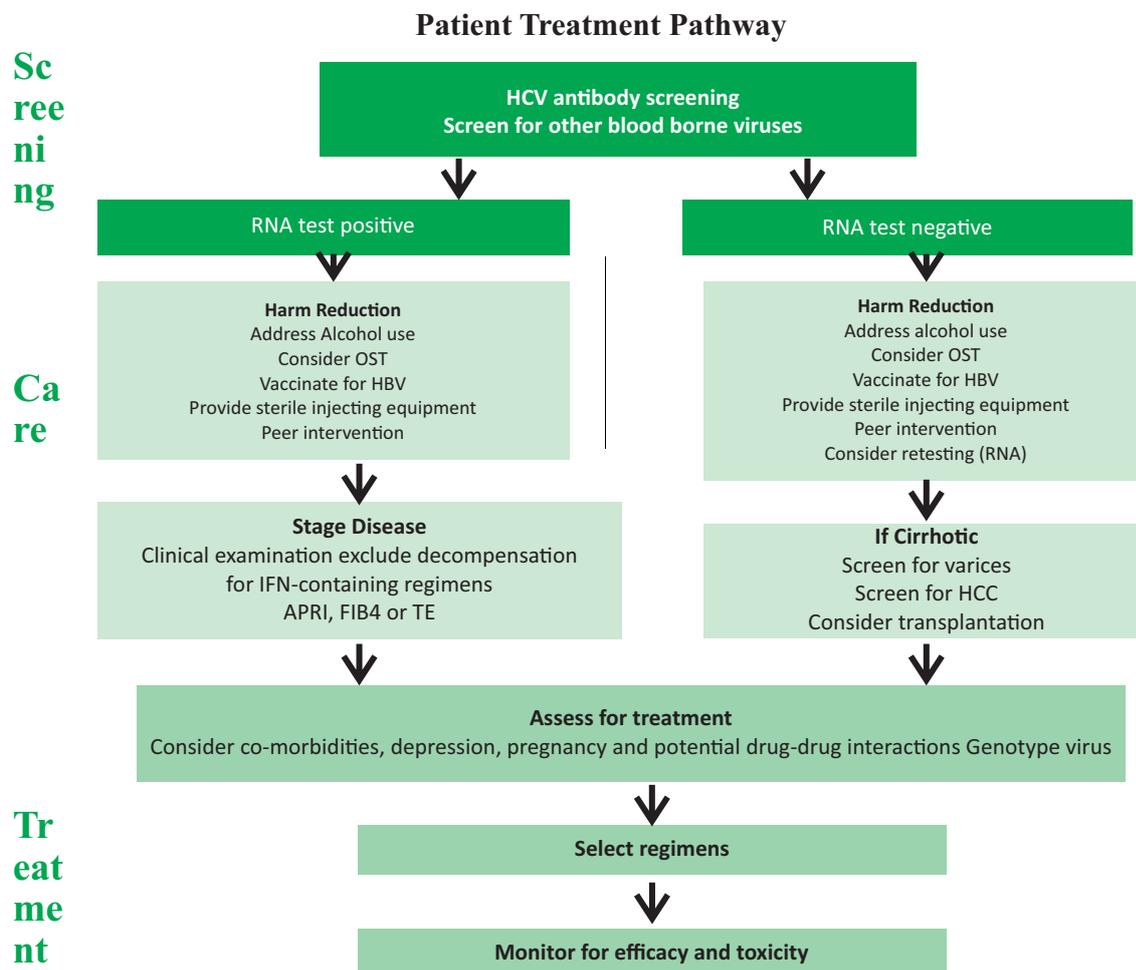
The majority (80%) of HCV infections progress to Chronic Liver Disease (CLD). Outcomes vary widely from subclinical infection to end stage liver diseases (ESLD, 20%) and liver cancer (5%). The more advanced the liver fibrosis, the more severe the disease outcomes. Management of HCV infection requires a comprehensive strategy to prevent and control HCV infection and related chronic liver disease.

3.1 GOALS OF MANAGEMENT

The general goals of management include the following:

- To achieve a sustained virologic response (SVR) or cure where possible
- To prevent liver disease progression to cirrhosis, liver failure and hepatocellular carcinoma
- To prevent transmission of HCV infections
- To improve quality of life.

A detailed pathway to be followed for the management of hepatitis C is shown in figure 3.1 below



3.2 HCV diagnosis

1. Screening:

Detection of HCV antibodies is the first step to diagnosis. Screening is conducted on whole blood, serum or plasma specimen, using rapid test or Enzyme Immunoassay (EIA) kits that are approved by NAFDAC and other stringent regulatory authorities (FDA, WHO).

Who to screen:

- Persons with past history of blood or blood products transfusion or organ transplant
- People who inject drugs (PWID)
- Persons with a history of haemodialysis
- Infants born to HCV positive mothers
- Contacts of HCV infected persons
- Health care workers especially those with known history of needle sticks/sharps exposure
- Clinical evidence of chronic liver disease or abnormal liver enzyme tests
- Persons living with HIV (PLHIV)
- Patients with tattoos, scarification marks, or other local surgical procedures
- Men who have sex with men (MSM), Female sex workers (FSW), and persons with a history of incarceration

2. Confirmation (Virologic evaluation of HCV infection):

Approximately 15–25% of persons who are infected with HCV will spontaneously clear the infection and do not develop chronic infection. These persons are HCV Ab seropositive but no longer infected with HCV. A nucleic acid test (NAT) for HCV RNA, which detects the presence of virus, is needed to distinguish persons with chronic HCV infection from those who have cleared the infection. NAT for HCV RNA is important prior to commencing and during treatment to assess treatment response. NAT can include RNA quantitative or qualitative testing for the detection of HCV RNA and should be performed directly following a positive HCV serological test to establish the diagnosis of chronic HCV infection.

3. HCV RNA Genotyping:

There are six HCV genotypes. (Genotype 1-6) In a HCV RNA positive person, the HCV genotyping should be done to determine optimal treatment **only if** pan-genotypic treatment regimens are un-available.

3.3 Assessment of Liver disease

3.3.1: Clinical Evaluation

A detailed history and physical examination of patients is required. Alcohol, drugs and history of other risk factors are evaluated. Physical examination is conducted to evaluate for features of chronic liver disease such as jaundice, hepatomegaly, splenomegaly and GI bleeding. The presence of ascites is highly suggestive of decompensated liver cirrhosis. These patients should be considered for treatment prioritization and referred for specialized care.

3.3.2: Assessment of hepatic injury /severity

1. Liver enzymes and other tests of liver function:



Liver enzymes include aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP). Other tests of liver synthetic function and/or portal hypertension include serum albumin, bilirubin, platelet count and prothrombin time. A progressive decline in serum albumin concentrations, rise in bilirubin, ALT, AST, ALP and prolongation of the prothrombin time are characteristically observed as decompensated cirrhosis develops.

2. Haematological test:

Full blood count (including platelets count) and test of coagulation such as Prothrombin Time and International Normalized Ratio (INR)

3. Liver Imaging; to evaluate hepatic parenchyma, intra hepatic masses and adnexa

- Ultrasound scan
- CT scan where applicable/necessary

3.3.3: Non-invasive tests (NITs) for Liver Fibrosis Assessment

Non-invasive methods for assessing the stage of liver disease are supplanting liver biopsy and have been validated in adults with Chronic HCV. Blood and serum markers for fibrosis, including APRI and FIB-4, as well as commercial markers such as Fibro Test can be estimated, or transient elastography (Fibro Scan) performed to rule out advanced fibrosis.

APRI Score and Liver Fibrosis Assessment:

Aspartate aminotransferase (AST)-to-Platelet Ratio Index (APRI) is a simple index for estimating hepatic fibrosis based on a formula derived from AST and platelet concentrations. For the purpose of early initiation of patients on therapy, the cutoff of 1.0 should be considered. APRI and FIB-4 scores are easily calculated using standard clinical labs. Below is the formula to be used for APRI Score:

APRI and FIB 4 Score calculation:

$$APRI = \frac{\frac{AST \text{ Level}}{AST \text{ (Upper Limit of Normal)}}}{Platelets \text{ Count } (10^9)/L} \times 100$$

NB: In this formula, the Platelets Count is expressed in thousands of platelets per microliter. So, if a patient has 137,000 platelets/ μ l, we would use 137 as the denominator of the formula.

$$FIB-4 = \frac{Age \text{ [years]} \times AST \text{ [IU/L]}}{(platelets \text{ [}10^9/L\text{]} \times \sqrt{ALT \text{ [IU/L]}}).16$$



ALT - alanine aminotransferase IU - international unit AST - aspartate aminotransferase ULN - upper limit of normal

An online calculator can be found at: <http://www.hepatitisc.uw.edu/page/clinical-calculators/apri>

Table 3.1. Low and High cut-off values for the detection of significant cirrhosis and fibrosis

	APRI (low-cut off)	APRI (high cut - off)	FIB4 (low cut - off)	FIB4 (high cut - off)	Transient elastography (Fibroscan)
Significant fibrosis (METAVIR = F2)	0.5	1.5	1.45	3.25	7-8.5kPa
Cirrhosis (METAVIR F4)	1.0	2.0	-	-	11-14kPa

Table 3.2. Summary of sensitivity and specificity of APRI, FIB4 and Fibroscan for the detection of advanced cirrhosis and fibrosis (all values are percentages)

		APRI (low-cut off)	APRI (high cut-off)	FIB4 (low cut - off)	FIB4 (high cut-off)	Transient elastography (Fibroscan)
Significant fibrosis (METAVIR ≥ F2)	Sensitivity (95% CI)	82 (77-86)	39 (32-47)	89 (79-95)	59 (43-73)	79 (74-84)
	Specificity (95% CI)	57 (49-65)	92 (89-94)	42 (25-61)	74 (56-87)	83 (77-88)
Cirrhosis (METAVIR F4)	Sensitivity (95% CI)	77 (73-81)	48 (41-56)	-	-	89 (84-92)
	Specificity (95% CI)	78 (74-81)	94 (91-95)	-	-	91 (89-93)

3.3.4: Liver biopsy

Liver biopsy has been used to ascertain the degree of necroinflammation and fibrosis, and to help guide the decision to treat. There are several established methods of scoring histology and measuring activity (necroinflammation) separately from staging (fibrosis).

Limitations of biopsy include sampling error, subjectivity in reporting, high costs, the risks of bleeding and pneumothorax, discomfort to the patient, and the need for training and infrastructure in LMICs. Liver biopsy findings should be categorized into mild, moderate or severe chronic necroinflammation.

Using the METAVIR group scoring system:

Fibrosis is staged on a scale of F0 to F4, as follows;

- F0 = no fibrosis.
- F1 = portal fibrosis without septa.
- F2 = few septa (moderate fibrosis).
- F3 = numerous septa without cirrhosis (advanced fibrosis).



- F4 = cirrhosis.

Significant fibrosis is defined by the presence of F2, F3 or F4

3.4 ANTIVIRAL THERAPY

Antiviral therapy is the cornerstone of treatment of chronic HCV infection. With the arrival of new antiviral therapies, a high rate of sustained virologic response (SVR) is possible in almost all patients.

3.4.1: Goal of Antiviral Therapy

The goal of antiviral therapy in patients with chronic HCV is eradication of HCV RNA, which is predicted by attainment of SVR. SVR is defined as aviremia 12 or 24 weeks after completion of antiviral therapy. An SVR confers a 97 to 100 % chance of being HCV RNA negative during long-term follow-up and can therefore be considered as virologic cure of HCV infection. SVR has been associated with decrease in all-cause mortality, liver-related death, need for liver transplantation, hepatocellular carcinoma, and liver-related complications even among those patients with advanced liver fibrosis.

3.4.2: Evaluation for Antiviral Therapy in HCV

1. All patients with HCV infection (confirmed with HCV RNA) should be treated.
2. However, if prioritization is necessary, refer to the table below.

Table 3.3. Indications for treatment of chronic hepatitis C: Who should be treated and when?

Treatment Priority	Patient group
Treatment is indicated	<ul style="list-style-type: none"> • All treatment-naïve and treatment-experienced patients with compensated and decompensated liver disease
Treatment should be prioritized	<ul style="list-style-type: none"> • Patients with significant fibrosis or cirrhosis, APRI score ≥ 1.0 (or equivalent Metavir score of F3 or F4) including decompensated cirrhosis • Patients with HIV co-infection • Patients with HBV co-infection • Patients with an indication for liver transplantation • Patients with HCV recurrence after liver transplantation • Patients with clinically significant extra-hepatic manifestations • Patients with debilitating fatigue • Individuals at risk of transmitting HCV (active injection drug users, men who have sex with men and high-risk sexual practices, women of child bearing age who wish to get pregnant, haemodialysis patients, incarcerated individuals)
Treatment should be considered	<ul style="list-style-type: none"> • Patients with APRI score < 1 (or equivalent METAVIR score of F0 -F2)
Treatment is justified	<ul style="list-style-type: none"> • Patients with moderate fibrosis (F2)
Treatment can be deferred	<ul style="list-style-type: none"> • Patients with no or mild disease (F0-F1) and none of the above-mentioned extra-hepatic manifestations
Treatment is not recommended	<ul style="list-style-type: none"> • Patients with limited life expectancy due to non liver related comorbidities



3.5 TREATMENT

3.5.1: Pre-treatment Counselling

In order to improve compliance HCV counselling before commencement of HCV treatment should include;

1. The health implications of chronic HCV infection (liver failure, cirrhosis, Liver cancer)
2. The chronic nature of the disease – monitoring may be lifelong
3. The possibility that spouse(s), children and close relatives may be infected and the need to screen and protect if uninfected
4. The need to avoid further health risks such as alcohol, herbal concoctions, aflatoxins (mouldy groundnuts), multiple sexual partners, tattooing, and scarification procedures (to avoid risk of co-infections and possibly re-infection)
5. The financial implications of treatment options in relation to the desired goal of treatment
6. The potential side effects of treatment options
7. The objectives and likely outcomes of treatment in regards to virologic response, normalization of liver function, prevention/reduction in the risk of further liver damage and liver cancer
8. The potential drug-drug or drug-food interactions (see appendix)

3.5.2: Treatment Options

There are many drugs approved for the treatment of Hepatitis C as shown in Table 3.4, which include all oral DAA therapy and interferon based regimen. Treatment regimens and duration depend on the presence or absence of liver cirrhosis in the patient, the viral genotype (for genotype specific regimens), and other factors that may complicate therapy. Several treatment regimens are available (see Table 3.5).

Interferon based regimen are characterized by significant adverse events (flu-like syndrome, anaemia, pancytopenia etc.), long treatment duration and lower efficacy rates. However, antiviral resistance does not occur.

DAAs have revolutionized HCV treatment and improved treatment outcomes. However, antiviral resistance may occur in rare instances. Pan-genotypic DAAs regimens are widely recommended as they provide high efficacy across all genotypes, have excellent safety profiles, and are administered orally. DAAs can be combined with Pegylated interferon to improve efficacy and reduce duration of treatment.



Table 3.4: Existing HCV Medicines and Dosage

Product	Presentation	Dosage
Sofosbuvir	Tablets containing 400mg of Sofosbuvir	One tablet once daily (morning)
Simeprevir	Capsules containing 150mg of Simeprevir	One capsule once daily (morning)
Daclatasvir	Tablets containing 30 or 60mg of Daclatasvir	One tablet once daily (morning)
Sofosbuvir/Ledipasvir	Tablets containing 400mg of Sofosbuvir and 90mg of Ledipasvir	One tablet once daily (morning)
Paritaprevir/Ombitasvir/Ritonavir	Tablets containing 75mg of Paritaprevir, 12.5mg of Ombitasvir and 50mg of Ritonavir	Two tablets once daily (morning)
Dasabuvir	Tablets containing 250mg of Dasabuvir	One tablet twice daily (morning and evening)
PegIFN- α 2a	Solution for injection containing 180, 135 or 90 μ g of PegIFN- α 2a	Once weekly subcutaneous injection of 180 μ g (or less if dose reduction needed)
PegIFN- α 2b	Solution for injection containing 50 μ g per 0.5ml of PegIFN- α 2b	Once weekly subcutaneous of 1.5 μ g/kg (or less if dose reduction needed)
Ribavirin	Capsules containing 200mg of Ribavirin	Two capsules in the morning and 3 in the evening if body weight < 75kg or Three capsules in the morning and 3 in the evening if body weight \geq 75kg

The choice of HCV treatment regimen should be individualized based on efficacy of treatment and response. However, for a public health approach, a simplified regimen with limited side effects, good efficacy, and oral route of administration is recommended.



Table 3.5. A list of preferred regimens:

PREFERRED REGIMENS FOR THE TREATMENT OF HEPATITIS C		
REGIMEN	FEATURES	MAJOR CONTRAINDICATIONS
Sofosbuvir/Daclatasvir	Highly efficacious across all genotypes and HIV+ patients	No clinically significant contraindication
	Affordable	
	Well tolerated, short duration, minimum SEs, AEs and drugs interactions	
Sofosbuvir/Ledipasvir (FDC)	Highly efficacious across most genotypes but not indicated for GT 2 & 3	No clinically significant contraindication
	Affordable	
	Well tolerated, short duration, minimum SEs, limited drugs interaction	
Sofosbuvir + Ribavirin	Acceptable cure rates across all genotypes	Pregnancy or unwillingness to use contraception
	More expensive and less tolerable than all-DAA regimens, but better than Peg-IFN	
	No risk of resistance	
	Can be used across all genotypes but with lower efficacy	Decompensated cirrhosis
		Uncontrolled depression or epilepsy
	Most Expensive	Pregnancy or unwillingness to use contraception
	Least tolerable regimen: injections, frequent SEs and AEs	Poorly controlled hypertension, cardiac failure or diabetes
		Abnormal Hematologic indices (see table 15), Serum Cr >1.5mg/dl
No risk of resistance	Breastfeeding	

Preferred regimen(s) for Public Health Approach (Without Genotyping)

Sofosbuvir + Daclatasvir

- 12 weeks (All Genotypes) for non-cirrhotic patients (APRI < 1.0)
- 24 weeks (All Genotypes) for cirrhotic patients (APRI ≥ 1.0)

Special Considerations for ART patients:

- Increase daclatasvir dosage to 90mg per day when co-administered with Efavirenz
- Decrease daclatasvir dosage to 30mg per day when co-administered with Atazanavir/Ritonavir
- Decrease daclatasvir dosage to 30 mg per day with the antibacterials clarithromycin, telithromycin, erythromycin and the antifungals ketoconazole, itraconazole, posaconazole and voriconazole



Sofosbuvir + Ribavirin:

- 24 weeks for all patients (All genotypes, non-cirrhotic and cirrhotic)
 - Of note, this is a sub-optimal regimen for certain genotypes based on SVR12 rates in clinical trials (AASLD/EASL/WHO treatment recommendations). However, with limited availability of DAAs, it remains a secondary option for Nigeria.

Table 3.6. Preferred regimen(s) if Genotype is available

A. Patients without cirrhosis (APRI <1.0)

Genotype	Sofosbuvir/ Daclatasvir	Sofosbuvir/ Ledipasvir	Sofosbuvir/ Ribavirin	PegIFN/Sofosbuvir/ Ribavirin
1	12 [A/E/S/W]	12[A/W]; 8-12*[E/S]		12 [E/S]
2	12 [A/E/S/W]		12 [A/E/S/W]	12 [E/S]
3	12 [A/E/S/W]		24 [A/E/S/W]	12 [A/E/S]
4	12[E/S/W]	12 [A/E/S/W]		12 [A/E/S]
5	12[E/S]	12 [A/E/S/W]		12 [A/E/S/W]
6	12[E/S]	12 [A/E/S/W]		12 [A/E/S/W]

Notes

A=AASLD 2016 HCV Treatment Guidelines (Treatment naïve patients only)

E=EASL 2015 HCV Treatment Guidelines

S=SOGHIN 2015 Treatment Guidelines

W=WHO 2016 HCV Treatment Guidelines

*8 weeks in treatment naïve if baseline HCV RNA below 6 million IU/ml

Sofosbuvir + Daclatasvir:

- All Genotypes= 12 weeks

Sofosbuvir + Ribavirin:

- Genotype 2= 12 weeks
- Genotype 3= 24 weeks

Sofosbuvir + Ledipasvir:

- Genotypes 1, 4, 5, 6= 12 weeks
- Genotype 1 can be treated for 8 weeks if treatment naïve and HCV RNA below 6 million IU/ml (EASL)



B. Patients with compensated cirrhosis (APR \geq 1.0)

Genotype	Sofosbuvir /Daclatasvir	Sofosbuvir /Daclatasvir/ Ribavirin	Sofosbuvir /Ledipasvir	Sofosbuvir /Ledipasvir /Ribavirin	Sofosbuvir/ Ribavirin	PegIFN/ Sofosbuvir/ Ribavirin
1	24 [A/E/S/W]	12[E/W]; 24 [A]	12[A]; [E/S/W]	24 12[W]; 12-24*[E]		12 [E/S]
2	12[E/W]; 16- 24 [A]; 24 [S]				16[W];16- 20[E/S];16- 24[A]	12 [E/S]
3	24[A/S]	24 [A/E/W]			24[A]	12 [A/E/S/W]
4	24[E/S/W]	12[E/W]	12[A]; 24[E/S/W]	12[W]; 12-24*[E]		12 [A/E/S/W]
5	24[E/S]	12[E]	12 [A]; 24 [E/S/W]	12[W]; 12-24*[E]		12 [A/E/S/W]
6	24[E/S]	12[E]	12 [A]; 24 [E/S/W]	12[W]; 12-24*[E]		12 [A/E/S/W]

Notes

A=AASLD 2016 HCV Treatment Guidelines (Treatment naïve patients only)

E=EASL 2015 HCV Treatment Guidelines

S=SOGHIN 2015 Treatment Guidelines

W=WHO 2016 HCV Treatment Guidelines

*Extension of treatment to 24 weeks if treatment experienced and negative predictors of response

Sofosbuvir + Daclatasvir

- All Genotypes= 24 weeks
- Genotype 2= treatment can shortened to 12-16 weeks
- *Special Considerations for ART patients (See Figure 2)*

Sofosbuvir + Daclatasvir + Ribavirin

- Genotype 1= 12-24 weeks
- Genotype 3= 24 weeks
- Genotypes 4, 5, 6= 12 weeks
- *Special Considerations for ART patients (See Figure 2)*

Sofosbuvir + Ledipasvir

- Genotypes 1, 4, 5, 6= 12-24 weeks
- *Special Considerations for ART patients (See Figure 2)*

Sofosbuvir + Ledipasvir + Ribavirin

- Genotypes 1, 4, 5, 6= 12 weeks (EASL recommends extending treatment to 24 weeks if treatment experienced and negative predictors of response such as platelet count $<75 \times 10^3$ /ul)
- *Special Considerations for ART patients (See Figure 2)*

Sofosbuvir + Ribavirin:

- Genotype 2= 16-24 weeks
- Genotype 3= 24 weeks



3.6 SPECIAL POPULATIONS

3.6.1 HIV and HCV co-infection

Assessment of potential drug-drug interactions is of critical significance in HIV-infected persons who are about to start HCV treatment. Careful consideration of such interactions is important to avoid toxicity and to ensure efficacy of the regimens used to treat both HIV and HCV in order to prevent the development of ARV resistance and increase likelihood of SVR. Reported interactions are updated on a regular basis and therefore consultation with a frequently updated database is strongly recommended

3.6.2 HBV and HCV co-infection

HBV/HCV: HBV and HCV co-infection may result in an accelerated disease course. In this instance, HCV is considered to be the main driver of the disease. Persons co-infected with HBV and HCV can be treated with antiviral therapy for HCV. SVR rates are similar to those of HCV mono-infected persons. After HCV clearance, there is a risk for HBV re-activation and this may require treatment with anti-HBV antiviral therapy

3.6.3 TB and HCV co-infection

Severe concurrent infections such as TB should generally be treated before commencing therapy for HCV. ART should be initiated with persons with HIV-associated TB as soon as possible, regardless of CD4 count. There are limited reported data on the co-management of persons co-infected with HCV, HIV and TB but such cases need sound clinical judgment in order to reduce the additive side-effects, pill burden and drug–drug interactions.

3.6.4 Persons with renal impairment

Both ribavirin and PEG-IFN require dose adjustment in persons with renal failure, and baseline testing of renal function is required before initiating therapy. Hepatic metabolism occurs for PEG-IFN α 2a, while PEG-IFN α 2b is renally cleared. While a theoretical accumulation of PEG-IFN α 2b could occur in persons with haemodialysis, no differences have been reported clinically. All oral DAAs are recommended in this group. However, there are no data regarding the safety of this medication among persons with renal impairment.

3.7 MONITORING AND FOLLOW-UP

3.7.1 Treatment Monitoring

Direct Acting Antivirals

DAA regimens are much better tolerated by patients, as they have fewer adverse events and less likely to be discontinued early

Recommendation:

Treatment monitoring is not generally required when using all-oral regimen, except in the following situations

- Renal impairment: If Sofosbuvir or Ribavirin based regimens are utilized in patients with chronic kidney disease, renal function should be monitored (Creatinine Clearance) as both exhibit renal clearance.



Dose Adjustments

- Ribavirin:
 - Moderate (30-50mL/min)=Alternating doses of 200mg and 400mg every other day
 - Severe (<30mL/min)= 200mg/day
 - ESRD= 200mg/day
- *Note: Sofosbuvir/Ribavirin only recommended for GT 2, 3 as above if genotype known.
- Sofosbuvir:
 - Mild-moderate (30-80mL/min)= No dose adjustment
 - Severe and ESRD= Not recommended
- Ribavirin based regimens: Severe hemolytic anemia with significant initial drops in haemoglobin may occur; therefore careful monitoring should be initiated.
- Direct monitoring of viral replication through NAT (Viral load) testing is not recommended
- Complex patients in specialist care may require more advanced chemistry and haematology monitoring

Pegylated interferon

For pegylated interferon based regimens, the following monitoring tests are recommended

- Monthly haematological and biochemical profile
- Three monthly Thyroid Function Tests
- Monthly evaluation for depression

Patients on pegylated interferon based regimen should be monitored closely for adverse effects as well as response to therapy. Tests to help monitor drug toxicity include the following:

- Complete blood count with differential
- Renal function testing
- Liver function tests (including alanine aminotransferase [ALT] level)
- Thyrotropin level

3.7.2 Confirmation of efficacy

Confirmation of SVR can be done with qualitative or quantitative NAT post-treatment to evaluate virologic response to therapy.

- DAA Regimens: testing at 12 weeks post-treatment (SVR12)
- Interferon-based regimens: testing at 12 weeks post-treatment (SVR12)

Patients who do not achieve SVR should be referred to a specialist and evaluated for re-treatment

3.7.3 Follow-up

Patients with decompensated cirrhosis and HBV/HCV co-infected patients should be referred to specialist centers.

Assessment and follow up for the progression of disease and for evidence of HCC is an essential part of the care of persons with HCV-related cirrhosis. Compensated cirrhosis may also progress over time to decompensated cirrhosis associated with ascites, oesophageal and gastric varices, and eventually to liver failure, renal failure and sepsis, all of which are life-threatening. The diagnosis of decompensated liver disease is based on both laboratory and clinical assessment, and therefore a careful medical examination of patients must be made before starting treatment. Persons with cirrhosis (including those who have achieved SVR) should be screened for HCC with



six-monthly ultrasound examination and α -fetoprotein estimation, and should have endoscopy every 1-2 years to exclude oesophageal varices.



3.8 – PROGRAMMATIC APPROACH TO HCV MANAGEMENT

3.8 □ PROGRAMMATIC APPROACH TO HCV MANAGEMENT

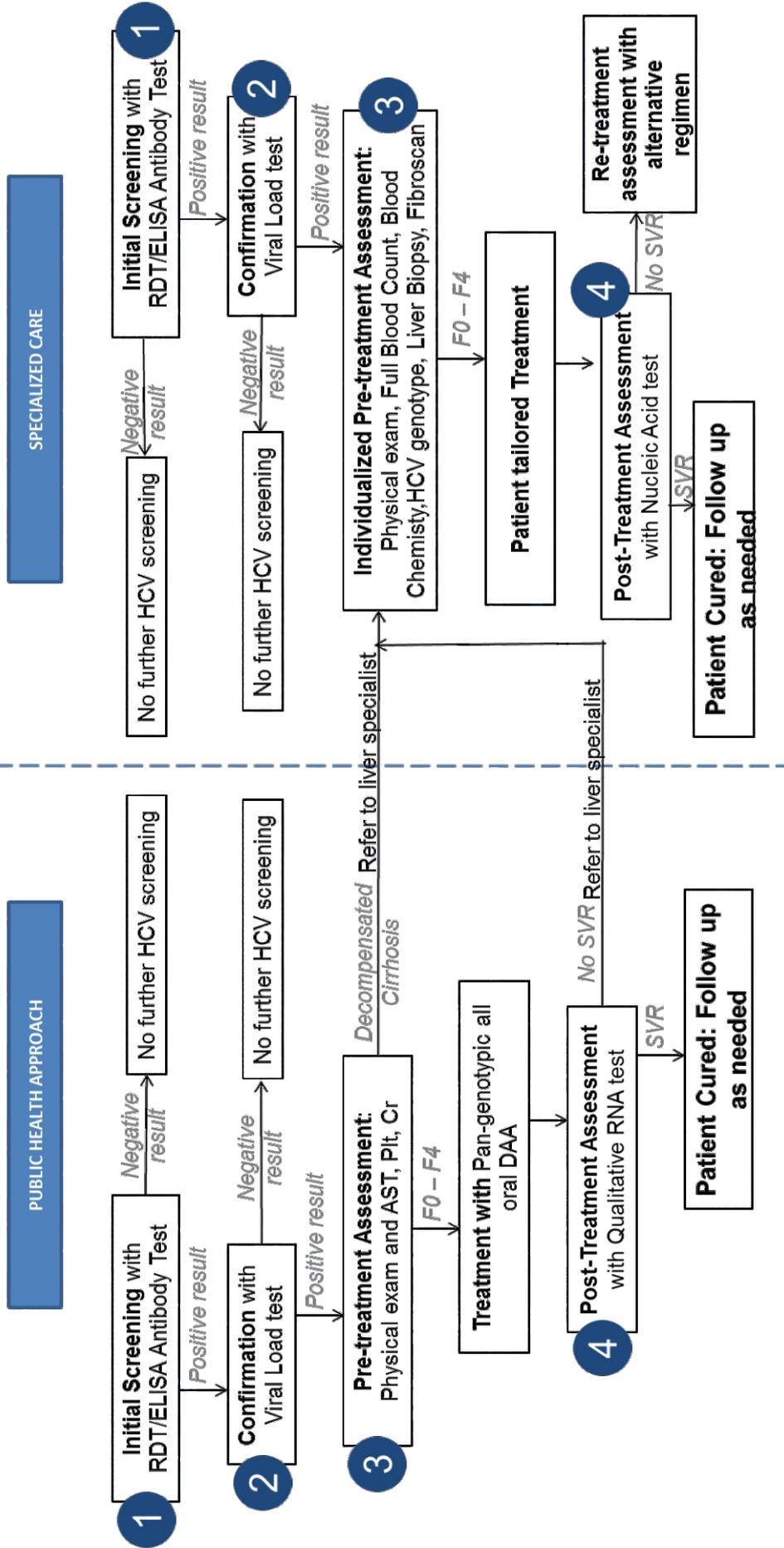


Table 3.7. Implementing the public health approach in HCV therapy

Item	Protocol Section	Specialized Standard of Care Lab Description	Included in public health approach (Yes/No)	Implementation modalities
1	Pre-treatment Screen	Hepatitis C antibody (Serum HCV Ab)	Yes	The HCV Ab can be performed using an ELISA assay or rapid test. A number of rapid tests are available with differing performance characteristics, such as sensitivity and specificity; which should be considered during selection of screening tests.
2	Pre-treatment Assessment	Qualitative /quantitative HCV RNA	Yes	Confirmation of chronic HCV is required secondary to false positives during initial screening as well as clearance of previous HCV infection. As with screening tests, NAT performance characteristics should be considered in selection of confirmatory testing platforms.
3	Pre-treatment Assessment	Physical Exam: Blood pressure, heart rate, pulse, cardiac, respiratory, abdominal, and neurological exam	Yes	Physical examination allows for evaluation of advanced liver disease (decompensated cirrhosis) manifested by evidence of bleeding from varices in the stomach or esophagus, jaundice, ascites (fluid in abdomen), edema of the lower extremities, and mental changes. Individuals with evidence of decompensated cirrhosis will be referred to a liver specialist for management.
4	Pre-treatment Assessment	HCV Genotype and subtype	No	A pan-genotypic regimen should be adopted.
5	Pre-treatment Assessment	Platelet Hepatic Function Panel: Albumin Bilirubin Alkaline phosphatase Alanine aminotransferase and aspartate aminotransferase	Yes- AST, Plt No- Alb, Bili, Alk Phos, ALT	AST and Plt allows for calculation of APRI score (AST to Platelet ratio index). APRI is a non-invasive measure of liver damage (advanced scarring (fibrosis) or cirrhosis) and guides treatment duration and ongoing management of liver disease post-SVR. Referral to specialists is not required for patients with APRI>1 and no signs of decompensation, but when/where available should result in liver cancer screening for advanced liver disease (ascites, encephalopathy, GI bleeding) and referral to tertiary treatment centers for evaluation by specialists.
6	Pre-treatment Assessment	Creatinine/Calculated glomerular filtration rate (GFR): Measure of kidney function.	Yes	One of the medications used in this protocol (sofosbuvir) is renally cleared and there is currently limited safety data in patients with poor kidney function. A GFR <30 ml/min would be an indication to consider delay in therapy until more safety data is available or other regimens are available.
7	Post-treatment Assessment at week 24 (End of Treatment + 12 Weeks)	At Week 24 (12 weeks after ending treatment): Qualitative HCV RNA	Yes	Measurement of sustained virological response (SVR) is recommended at 12 weeks post treatment. If there is no HCV detected in the blood 12 weeks after finishing treatment, the patient has achieved SVR 12 and is considered cured.
8	Post-treatment Assessment at week 24	At Week 24 (12 weeks after ending treatment): HCV Genotype and subtype	Maybe	If SVR12 is not achieved, HCV genotyping and subtyping is recommended. This occurs in a minority of patients; assuming the cost of genotyping at this point significantly decreases overall treatment costs while providing information requisite for future retreatment.



3.9 PREVENTION

To reduce the number of Hepatitis C infections and HCV-related diseases, it is necessary to implement primary, secondary and tertiary prevention methods. Primary prevention methods reduce the risk of contracting the infection. Secondary prevention aims to identify disease at the earliest stage to reduce the impact of disease after it has occurred. Tertiary prevention aims to reduce the impact of on-going illness that has lasting effects.

3.9.1 Primary Prevention Methods

Primary prevention activities reduce the potential risk for HCV transmission from blood, sexual intercourse with infected persons, and exposure to needles (drugs, tattoos, piercings).

Precautionary measures should include;

- Educating the public on HCV and modes of transmission and infection
- Not sharing razors, toothbrushes, manicure tools and other items that could be contaminated with blood
- Making sure that sterile equipment is used when getting a tattoo or piercing
- Never sharing IV drug needles or other drug equipment
- Counselling and education to prevent initiation of injecting drugs or risky sexual practices, especially for adolescents
- Counselling those who are at risk for sexually transmitted diseases and drug-related infections on what those individuals can do to minimize their risk of becoming infected

Individuals who use illegal drugs should be advised to;

- Stop using and injecting drugs
- Enter and complete a substance-abuse treatment
- Never share needles If drug use is continued
- Use sterile equipment and clean the site of injection
- Get vaccinated against Hepatitis A and Hepatitis B

Individuals who are at risk for STDs should be advised to;

- Have sex with only one uninfected partner or not to have sex at all
- Use condoms correctly and every time to protect themselves and their partner
- Get vaccinated against Hepatitis B
- If there is a risk for infection, individuals should be routinely tested

3.9.2 Secondary Prevention Methods

Secondary prevention activities reduce risks of chronic disease by identifying the HCV infected individuals through testing and by providing appropriate medical treatments. Methods that should be done include;

- Counselling patients infected with HCV about the disease, treatment methods and what can be done to prevent transmission to other individuals
- Diagnosing at which stage the infection is and implementing appropriate treatment

Precautions that can be taken to prevent the spread of HCV in a hospital setting;

- For transfusion and transplants, thorough screening of the blood is necessary to make sure it is not infected
- Personal protective equipment should be worn at all times by the hospital staff when



dealing with the patients

- Washing hands after and between patients is necessary
- Sharing of non-disposable items between patients should be avoided
- Getting vaccinated against Hepatitis B

Currently, there is no vaccine against HCV because the high mutability of the virus complicates vaccine development.

3.9.3 Prevention of Hepatitis C among at risk populations

- Ensuring safe injection practices in healthcare and community settings
- Ensure safe transfusion of blood and blood products
- Promotion of correct and consistent condom use
- Routine screening of sex workers in high-prevalence settings
- Offer peer education interventions to people who inject drugs to reduce the incidence of viral hepatitis
- Integrated action to eliminate discrimination and gender violence, and to increase access to Medical and social services



CHAPTER FOUR

CARE AND SUPPORT

4.1 DEFINITION

Care and Support, in the context of viral hepatitis B and C, means catering to the needs of people infected with viral hepatitis B and C and providing appropriate support for them, their families and caregivers. Care and Support adds to the holistic, facility based, multidisciplinary and patient-focused care for persons infected.

4.2. CARE AND SUPPORT FOR PEOPLE INFECTED WITH HBV & HCV

4.2.1 Nutritional Support

People with viral hepatitis will thrive best on a balance diet and may need nutritional support to achieve this. However this cannot take place of specific antiviral terrapy Discussed in chapters 2 and 3 above.

The patients should be counselled on the following:

- The need for adequate intake of energy and protein rich foods, fruits and vegetables
- The need for micronutrient supplementation, .
- These micronutrients may enhance the immune status of the patients. They may be found in dark green leafy vegetables, yellow and orange fruits, sweet potatoes, pumpkins, carrots, avocado and tomatoes.
- Patient should be counselled against using herbal medicines as the specific treatment for viral hepatitis
- In situation where chronic Hepatitis B and C has been established, iron supplementation should be discouraged.
- Fatty food should be discouraged.
- Obesity should be discouraged as steatosis may worsen the effect of HCV infections

4.2.2 Lifestyle and Behavioural Change

Behavioural changes that should be encouraged to reduce risk of progression to chronic liver disease and transmission of hepatitis viruses include:

- Cessation of alcohol, smoking, foods containing aflatoxins and recreational drug use

In addition,

- People infected with the hepatitis viruses should be counselled on how to deal with stress and live a healthy lifestyle.
- They should be counselled on how to avoid transmitting the virus to others

4.2.3 Specific Considerations for Viral Hepatitis Positive Pregnant Women

- Hepatitis B screening should be routine during antenatal visit.
- Pregnant women positive for HBV infection should have viral load done in their 3rd trimester and treated with Nucleoside Analogues to reduce the chance of MTCT.



- Babies born to Hepatitis B positive mothers should have Hep B immunoglobins at birth and first dose of monovalent Hep B vaccine within 24 hours of birth.

4.2.4 Disclosure of Hepatitis Status to Children

Disclosing hepatitis infection status to children is a sensitive issue, which must consider the needs, feelings, age, beliefs and understanding of the child and caregiver. It must however be done to improve outcomes in the treatment and care of children.

Importance of Disclosure to Children

- Reduction of developing myths about their infection
- Improvement of access to care and support services
- Enhancement of adherence to treatment and coping strategies
- Reduction of negative psychosocial impact
- It helps to reduce the risk of transmission

Counselling for disclosure in children

This involves counselling the caregivers to support age-appropriate hepatitis infection status disclosure to the child with minimal negative impact. Parents who decline or fail to disclose to their children should be counselled on the importance of the child knowing his/her status, and assisted to do so.

Steps for Counselling hepatitis infected Children and their Families

- Evaluate the child and family for readiness-including child's age and maturity. Five to seven years are earliest recommended ages for disclosure, and all should be disclosed by age 12.
- Ascertain a child's and caregiver's understanding of hepatitis infection
- Explain the benefits of early awareness of hepatitis infection to the child and caregiver/family
- Provide on-going psychosocial support.

4.3 IMMUNIZATION

Immunization is an effective way of preventing diseases. Immunizations should be given according to the national immunization schedule. Adults with HCV infection who are hepatitis B negative should have the standard three doses of hepatitis B vaccine.

Human Immunoglobulin (HBIG) as a passive immunization should be made available to those exposed to the virus, and who are hepatitis B negative.

4.4 UNIVERSAL SAFETY PRECAUTIONS

All health facilities in the private and public sector should adopt a policy for the prevention of accidental occupational exposure to blood borne pathogens.

Minimum Standards of Universal Safety Precautions to be observed by health workers include:

- Routine hand washing with soap and water before and after contact with any patient
- Use of barrier precautions eg PEP
- Safe handling and disposal of sharp instruments and equipment, including needles and syringes



- Strict adherence to injection principles
- Do no harm to Self, to the client and to the Community

Materials should be provided for universal precautions. The minimum materials/equipment to be provided include:

- Liquid soap from a dispenser or container
- Running water or a bucket with tap kept full with clean water or a ladle for dipping, if running water is not available
- Single-use towels (paper towels, or cloth towels that will be used once and laundered). If not available, hands should be air-dried.
- SOPs and Job aids to educate personnel on susceptibility to hepatitis virus infection and means of prevention

4.5 Linkages, Networks and Referral Services

Referral is the process by which client needs for treatment, care and support services are assessed and prioritized, and clients are provided with assistance in accessing such services. Referral should also include proactive actions necessary to facilitate initial contact with treatment, care and support service providers. Patients who are screened in primary health centres should have access to treatment and more advanced services in secondary and tertiary level facilities.

Reasons for referral

Clinical services

These include clinical evaluation and management, monitoring the progression to liver disease, more advanced investigation and monitoring for development of HCC Hepato Cellular Carcinoma.(HCC)

Social/Legal support services

Clients who test positive may require legal and/or social services for counselling on how to prevent or deal with discrimination in school, employment, housing and public accommodation.

Community Awareness, Engagement and Participation

The burden of Hepatitis virus diseases is very heavy in Nigeria and to effectively drive the prevention, control and management efforts, and intensification of social mobilization, communication, advocacy, community participation and community engagement strategies at National, State, LGA and Ward levels is very imperative.

It is also very necessary to identify key players/leaders at all levels for advocacy and social mobilization.

Advocacy

- key stakeholders to support Community mobilization to create awareness and demand for the interventions delivered.
- Traditional, religious leaders, NGOs, CBOs, women and youth associations and others as it relates to the area.

SOCIAL MOBILIZATION – Response to Prevention and Control of Hepatitis Virus Diseases

- Messages to change behaviours



- Community dialogues to interact with people to build trust and negotiate for ownership
- Advocacy to leaders to support efforts
- Identify and develop relationship, trust, credibility and sense of ownership with leaders.
- Identify all assets in the nation, state LGA and ward
- Develop appropriate key messages to the level of the audiences.

Communication

- TV,/ Radio drama, songs and music around the community
- Use of informants/educators (mobile public announcement tricycle)
- Rallies
- Road shows
- Use of OB Van to announce benefits, dates, age group and venue of the campaign.
- Identify key women groups to help mobilize their peers. This should include young women within the age group. E.g., FOMWAN, YWCA, etc.
- Identify key influencers / opinion leaders such as youth leaders, NYSC members etc to be part of the mobilization team.
- Develop appropriate key messages for the target age groups. IEC messages could help.
- Sensitization of the community pre and during implementation.
- Engagement of community leaders during micro planning process
- Mobilization of key opinion leaders in the area especially young women and husbands.
- Improve Interpersonal communication skills of Health workers and town announcers



CHAPTER FIVE

ADHERENCE TO ANTIVIRAL THERAPY

5.1 DEFINITIONS

Adherence is a term used to describe the patients' behaviour of taking drugs correctly based on mutual agreement between the patient and health care provider; it involves:

- Taking the right drugs
- The right dose
- The right frequency
- The right time

Adherence also means a patient attending all scheduled clinic visits. Adherence to antiviral treatment is an essential component of individual and programmatic treatment success. Adherence is crucial for delaying or preventing the development of drug resistance to some of the antiviral drugs. The measures to ensure optimal adherence should be undertaken at initiation and during therapy.

5.2 ADHERENCE PREPARATION FOR ANTIVIRAL THERAPY

The success of any adherence strategy depends on the education of patients before the initiation of treatment, an assessment of their understanding of and readiness for treatment. Adherence counselling includes giving basic information on hepatitis B and C infections and their manifestations, and the benefits and side effects of antiviral medications. It also includes how the medications should be taken and the importance of not missing any dose, what to do if doses are missed and steps to be taken to restart therapy if doses are missed. Information and education materials can be particularly useful in this process. Consideration should be given to the patient's lifestyle when possible, and may involve relatives, friends and/or community members as agreed with the patient.

5.3 ONGOING ADHERENCE FOR CLIENTS ON ANTIVIRAL THERAPY

It is essential to continue with adherence counselling. This should involve adherence assessments during every visit and post treatment follow up.

5.4. MEASUREMENT OF ADHERENCE

Virologic cure for HCV and functional cure for HBV are strongly dependent on adherence to taking the prescribed medications. Adherence in many studies is measured by expressing the number of doses taken as a percentage of the number of doses prescribed. Measurement methods include: patient self-report, pharmacy drug pick-up, pill count, questionnaire and electronic drug monitoring methods.



5.4.1 Factors known to improve Adherence

The following factors have been associated with high adherence rates:

- Increased access to Antiviral Therapy
- Individual patients, family, peers and friends, community members, or treatment-supporter engagement in adherence education
- Family-based care if more than one family member is infected
- Continuous and effective adherence counselling, including knowledge and understanding of hepatitis B and C infection, course of treatment, expected adverse reactions and management of such reactions.
- Drug regimen simplicity e.g. Fixed Drug Combination (low pill burden)

Shorter duration of therapy

- When possible use drugs with less adverse effects.

5.4.2 Factors Associated with Poor Adherence

- Poor patient-caregiver relationship
- Forgetfulness
- Depression
- Lack of patient education
- Drug toxicity
- Severe illness
- Pregnancy related conditions
- Incarceration
- Long duration of treatment
- Lack of social support
- Substance abuse
- Cost of treatment.

5.4.3 Strategies for Improving Adherence

- Treatment education for patients and involvement of treatment partners
- Routine assessment and reinforcement of adherence during follow up
- Fixed dose combination
- Reminders and patient engagement tools (e.g. drug calendars, pill boxes, a reminder call/SMS text messages, alarm clock)
- Positive feedback on health improvements
- Address adverse events
- Address life-style factors e.g. alcohol abuse Adapting therapy to the client's /patient's lifestyle
- Support groups
- Improved social support.



CHAPTER SIX

MANAGEMENT OF ADVERSE REACTIONS AND COMPLICATIONS OF ANTI HEPATITIS MEDICINES

The therapeutic benefits of medicines should always outweigh the risk. While the safety profiles for medicinal products have been established, adverse events (AEs) are not uncommon. AEs are often encountered with medicinal products in the course of prevention and patient management. AEs are identified and managed on time through effective Pharmacovigilance.

6.1 PHARMACOVIGILANCE; ADVERSE DRUG REACTION (ADR) AND ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, response and prevention of adverse drug reactions (ADRs) and other potential medicine-related problems including adverse events following immunization (AEFIs). A pharmacovigilance system is designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit ratio. A pharmacovigilance system like any system is characterised by its structures, processes and outcomes (refer to Good Vigilance Practice). The pharmacovigilance system should be in such a way that public health emergencies and preparedness plans are developed as appropriate.

Adverse Event (AE) is any untoward medical occurrence in a patient or clinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with the treatment.

An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Adverse drug reaction (ADR) is defined as a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of a disease, or for the modification of physiological function.

Adverse event following immunization (AEFI) is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. If not rapidly and effectively dealt with, can undermine confidence in a vaccine and ultimately have dramatic consequences for immunization coverage and disease incidence.

Reporting of ADR and AEFI requires structures and processes for the collection, recording and transmission of reports of suspected adverse reactions associated with medicinal products for human use to the National Pharmacovigilance Center. These can be achieved by ensuring all stakeholders adhere to their roles and responsibilities as shown in Table 12 below.



Table 12: Roles and responsibilities of stakeholders in the PV system for hepatitis

STAKEHOLDER	RESPONSIBILITIES
FMOH, SMOH, NPHCDA, SPHCDA, State NAFDAC Offices and NAFDAC Headquarters	<ul style="list-style-type: none"> • Strengthen facility based pharmacovigilance units to ensure that the collected reports are authentic, legible, accurate, consistent, verifiable and as complete as possible for clinical assessment. • Ensure consumers and Healthcare professionals have requisite knowledge to enable them report suspected AR and where necessary immediate investigation should be carried out to ascertain the authenticity of the information.
NPHCDA/ SPHCDA	<ul style="list-style-type: none"> • Establish systems to ensure counseling of all caregivers on AEFIs and pharmacovigilance. • Investigation backed with laboratory analysis and documentation
Marketing Authorization Holder (MAH)	<ul style="list-style-type: none"> • Establish mechanisms enabling the traceability of products and systems for the collection and reporting of ADRs/AEFIs, including follow-up of reports while complying with data protection principles. • Ensure that all ADR/AEFI information regarding medicinal products marketed by the MAH, within or outside Nigeria are reported to NAFDAC (refer to MAH guideline and PV policy).
Healthcare providers	<ul style="list-style-type: none"> • Assess patients for AE at every encounter and report all suspected adverse events using the ADR/AEFI reporting form.
Community/Individuals/CSOs/NGOs and patient groups	<ul style="list-style-type: none"> • Identify and report all AEs through designated channels (Health facilities, NAFDAC, SMOH, FMOH, SPHCDA, NPHCDA)
NAFDAC	<ul style="list-style-type: none"> • Receive, investigate, assess, provide feedback and archive information on ADR/AEFIs in compliance with the data protection requirements. • Establish systems for capacity



6.2 CLASSIFICATION OF ADVERSE DRUG REACTIONS

The World Health Organization classifies ADRs into four categories based on the severity grades. Severity is a subjective assessment made by the healthcare provider and/or the patient. Despite being subjective, it is useful in identifying adverse reactions that may affect adherence or that needs prompt intervention. The following guide can be used to estimate the severity grade of ADRs;

Table 13: WHO Severity Grading of ADR

Grade 1 – Mild ADR	Transient or mild discomfort (<48 hours) No limitation of activity No medical intervention or therapy required
Grade 2 – Moderate ADR	Mild to moderate limitation of activity Some assistance may be needed No or minimal medical intervention required
Grade 3 – Severe	Marked limitation of activity Some assistance usually required Medical intervention or therapy required Hospitalization possible
Grade 4 – Life Threatening ADR	Extreme limitation of activity Significant assistance required Significant medical intervention or therapy required Hospitalization or hospice care probable.

Vaccine reactions (AEFI) can be classified into two types:

1. Common, usually minor and self-limiting
2. Rare and serious

An AEFI is considered serious if: it results in death, is life-threatening, requires patient hospitalization or prolongation of existing hospitalization, it results in persistent or significant disability/incapacity, it results in congenital anomaly/birth defect or requires intervention to prevent permanent impairment or damage.



Common adverse events associated with hepatitis vaccinations are as follows;

<p>Hepatitis B vaccine</p>	<p>Nausea, vomiting, redness of the face, neck, arms, and occasionally, upper chest, drowsiness, sleeplessness, fatigue, pain and tenderness at injection site, pruritus, fever, dizziness, headache, vertigo, swelling at injection site, induration at injection site, erythema, ecchymoses, joint pain, skin rash or welts (may occur days or weeks after receiving the vaccine), blurred or other vision changes, confusion, difficulty in breathing or swallowing, dizziness, faintness or light headedness when getting up suddenly from a lying or sitting position, itching especially of the feet or hands, muscle weakness, numbness or tingling of the arms and legs, reddening of the skin, especially around the ears, sweating, swelling of the eyes, face, or inside of the nose, unusual tiredness or weakness (sudden and severe), Hard lump, unusual tiredness or weakness, muscle pain, agitation, back pain or stiffness in neck or shoulder, chills, constipation, diarrhea, difficulty with moving, feeling of warmth, general feeling of discomfort or illness, sore throat, runny nose, lack/decreased appetite, stomach cramps or pain, sudden redness of skin, swelling of glands in the armpit or neck, trouble with sleeping, unable to sleep, weight loss.</p>
<p>Hepatitis A vaccine</p>	<p>Tiredness, headache, loss of appetite, nausea, slightly raised temperature (normal temperature is 36-36.8°C), swelling and induration at injection site.</p>



Table 14: Common laboratory and clinical abnormalities associated with medicines for prevention and management of hepatitis

Tenofovir (TDF)	<p>Tubular renal dysfunction, Fanconi syndrome [Risk factors: Underlying renal disease; Older age; BMI <18.5 (or body weight <50 kg); Untreated diabetes mellitus; Untreated hypertension; Concomitant use of nephrotoxic drugs or a boosted PI],</p> <p>Lactic acidosis or severe, hepatomegaly with, steatosis, [Risk factors: Prolonged exposure to nucleoside analogues; Obesity],</p> <p>Exacerbation of hepatitis B (hepatic flares) [Risk factors: Discontinuation of TDF due to toxicity]</p> <p>Nervous system: Insomnia, headache, dizziness, depression, Fatigue, anxiety, peripheral neuropathy</p> <p>Dermatologic: Skin rash (includes maculopapular, pustular, or vesiculobullous); pruritus; or urticaria, pruritus, Diaphoresis</p> <p>Endocrine & metabolic: Hypercholesterolemia, increased serum triglycerides, Weight loss, glycosuria, hyperglycemia, lipodystrophy</p> <p>Gastrointestinal: Abdominal pain, nausea, diarrhea, vomiting, Increased serum amylase, anorexia, dyspepsia, flatulence</p> <p>Neuromuscular & skeletal: Decreases in bone mineral Density [Risk factors: History of osteomalacia and pathological fracture; risk factors for osteoporosis or bone loss], increased creatinine phosphokinase, weakness, Back pain, arthralgia, myalgia</p> <p>Miscellaneous: Fever</p> <p>Cardiovascular: Chest pain</p> <p>Genitourinary: Hematuria</p> <p>Hematologic & oncologic: Neutropenia</p> <p>Hepatic: Increased serum ALT, increased serum AST, increased serum transaminases, increased serum alkaline phosphatase</p> <p>Renal: Increased serum creatinine, renal failure</p> <p>Respiratory: Sinusitis, upper respiratory tract infection, nasopharyngitis, pneumonia</p> <p>Postmarketing and/or case reports: Angioedema, exacerbation of hepatitis B (following discontinuation), Fanconi's syndrome, hepatitis, hypersensitivity reaction, hypokalemia, hypophosphatemia, immune reconstitution syndrome, increased gamma-glutamyl transferase, interstitial nephritis, lactic acidosis, myopathy, nephrogenic diabetes insipidus, nephrotoxicity, osteomalacia, pancreatitis, polyuria, proteinuria, proximal tubular nephropathy, renal insufficiency, renal tubular necrosis, rhabdomyolysis, severe hepatomegaly with steatosis</p>
Entecavir	<p>Hepatic: Elevated ALT, post treatment exacerbation of hepatitis/ALT flare, deaths due to liver-related causes (e.g. hepatic failure, hepatic encephalopathy, hepatorenal syndrome, upper gastrointestinal hemorrhage; hepatic encephalopathy. On-treatment exacerbation of hepatitis/ALT flares, Elevated AST, lactic acidosis and severe hepatomegaly with steatosis (including fatal cases), severe acute exacerbations of hepatitis B (after discontinuation of therapy). Post treatment exacerbations of hepatitis or ALT flare other such as hepatic failure, hepatic encephalopathy, hepatorenal syndrome, and upper gastrointestinal hemorrhage.</p> <p>Hematologic: Decreased albumin (less than 2.5 g/dL), platelets (less than 50,000/mm³) with hepatic decompensation.</p>



	<p>Gastrointestinal: Elevated lipase, Diarrhea, dyspepsia, nausea, vomiting, elevated amylase, abdominal pain, upper gastrointestinal hemorrhage, peripheral edema, ascites, pyrexia/fever, fatigue, ascites, and pyrexia were reported in patients with hepatic decompensation</p> <p>Oncologic: Hepatocellular carcinoma, Malignant neoplasms,</p> <p>Renal: Creatinine increase of at least 0.5 mg/dL, increase serum creatinine of 0.5 mg/dL and renal failure were reported in patients with hepatic decompensation. Increased serum creatinine, Renal failure</p> <p>Respiratory: Upper respiratory infection, cough, nasopharyngitis, rhinitis</p> <p>Metabolic: Fasting hyperglycemia, decreased blood bicarbonate, Elevated alkaline phosphatase, lactic acidosis.</p> <p>Genitourinary: Hematuria, glycosuria, dysuria.</p> <p>Nervous system: Headache, dizziness, somnolence, insomnia</p> <p>Dermatologic: Erythema, photosensitivity with lethargy</p> <p>Musculoskeletal: Arthralgia, myalgia, back pain</p>
<p>Ribavirin</p>	<p>Respiratory: dyspnea, cough, pharyngitis, rhinitis, and sinusitis, pulmonary infiltrates, pneumonitis, pulmonary hypertension, pneumonia, sarcoidosis, and exacerbation of sarcoidosis. Mechanically ventilated patients may be predisposed to respiratory deterioration.</p> <p>Immunologic: Hypersensitivity reactions (urticaria, angioedema, bronchoconstriction, and anaphylaxis.)</p> <p>Dermatologic: Severe skin reactions including vesiculobullous eruptions, Stevens-Johnson syndrome, erythema multiforme, and exfoliative dermatitis/erythroderma) skin irritation from prolonged drug contact. Alopecia, pruritus dermatitis, dry skin, increased sweating, eczema, lichenoid eruptions and maculopapular rashes. Rash has been reported in patients treated with and health care workers exposed to aerosolized ribavirin. Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported during post marketing.</p> <p>Cardiovascular: angina, arrhythmia, and fatal and nonfatal myocardial infarctions, cardiac arrest, hypotension, bradycardia, bigeminy, tachycardia, hypertension, digitalis toxicity and congenital heart disease.</p> <p>Hematologic: anemia, lymphopenia, neutropenia, thrombocytopenia and leukopenia. Aplastic anemia and thrombotic thrombocytopenic purpura, pancytopenia (marked decreases in red blood cells, neutrophils, and platelets)</p> <p>Ocular: blurred vision, corneal ulcer, Conjunctivitis, Eye irritation, Lacrimation, damage to contact lenses.</p> <p>Gastrointestinal: nausea and vomiting, diarrhea, vomiting, abdominal pain, dry mouth, dyspepsia, constipation, Peptic ulcer, gastrointestinal bleeding, pancreatitis, and colitis.</p> <p>Musculoskeletal: myalgia, arthralgia, musculoskeletal pain, and back pain, Myositis.</p> <p>Nervous system: headache, dizziness (excluding vertigo), memory impairment, Peripheral neuropathy, coma, cerebral hemorrhage, Taste perversion, Hearing impairment, hearing loss.</p> <p>Metabolic: anorexia, weight decrease, Diabetes mellitus, Dehydration, falsely low hemoglobin A1c levels.</p> <p>Psychiatric: irritability/anxiety/nervousness/emotional lability, insomnia, depression, concentration impairment, mood alteration, and agitation. Suicide, suicidal ideation, psychosis, aggression, anxiety, drug abuse/overdose, psychotic disorder, and</p>



	<p>hallucination Endocrine: hypothyroidism General: fatigue, pyrexia, myalgia, headache, and rigors, Fatigue/asthenia, pyrexia, rigors, chills, influenza-like illness, unspecified pain, right upper quadrant pain, pain, chest pain, malaise, Hyperuricemia in association with hemolysis and flushing. Hepatic: hepatic dysfunction, fatty liver, cholangitis, Hyperbilirubinemia, hepatomegaly and ALT. Immunologic: sepsis, osteomyelitis, endocarditis, pyelonephritis, pneumonia, sarcoidosis, systemic lupus erythematosus, rheumatoid arthritis, Resistance mechanism disorders, including viral infection, fungal infection. Genitourinary: Menstrual disorder.</p>
<p>Pegylated Interferon</p>	<p>Nervous system: Dizziness, headache, concentration impairment, Vertigo, syncope, migraine, memory impairment, weakness, hypoesthesia, hyperesthesia, paresthesia, tremor, taste disturbance, somnolence, tinnitus, Influenza-like signs/symptoms, fatigue/asthenia, pyrexia, fatigue, rigors, asthenia, pain, overall resistance mechanism disorders, Fever, chills, chest pain, influenza-like illness, malaise, lethargy, shivering, hot flushes, thirst, infections (fungal, viral, bacterial), peripheral edema, flushing, earache. Musculoskeletal: back pain have been reported in CHC patients. Myalgia, arthralgia, arthritis, muscle weakness, neck pain, musculoskeletal pain and muscle cramps Hematologic: Neutropenia, anemia, lymphopenia, Thrombocytopenia, lymphadenopathy, Neutropenia, anemia and thrombocytopenia Gastrointestinal: Nausea/vomiting, diarrhea, abdominal pain, dry mouth, dyspepsia, Nausea, diarrhea, nausea/vomiting, abdominal pain, vomiting, upper abdominal pain, dysphagia, mouth ulceration, gingival bleeding, glossitis, stomatitis, flatulence, gastritis, gingivitis, cheilitis, constipation and oral candidiasis</p> <p>Psychiatric: Insomnia, irritability/anxiety/nervousness, irritability, depression, anxiety, Concentration impairment, mood alteration, nightmares, aggression, emotional disorders, nervousness, decreased libido, affect lability, apathy, Impairment of desire, sexual satisfaction affected (potentially) and sexual dysfunction Dermatologic: Alopecia, pruritus, dermatitis, dry skin, increased sweating, rash and eczema combination therapy, dry skin, Common: Increased sweating, eczema, psoriasis, urticaria, skin disorder, photosensitivity reaction, night sweats, herpes simplex, lipodystrophy, Injection site reactions and cutaneous necrosis.</p> <p>Hepatic: Elevated ALT Metabolic: Anorexia, weight decrease, decreased appetite and Hyperlactacidemia/lactic acidosis Respiratory: Dyspnea, cough and exertional dyspnea Immunologic: autoimmune phenomena include hypothyroidism, sarcoidosis, systemic lupus erythematosus, rheumatoid arthritis, immune thrombocytopenic purpura, thyroiditis, psoriasis. Cardiovascular: Tachycardia, palpitations, Ocular: Blurred vision, eye pain, eye inflammation, xerophthalmia Post marketing reports: Serous retinal detachment Endocrine: Hypothyroidism, abnormal thyroid laboratory values</p>



	<p>Genitourinary: Chromaturia, Impotence, chromaturia Hypersensitivity: Anaphylaxis, Anaphylactic shock</p>
Sofosbuvir	<p>General: Fatigue, asthenia, pyrexia, chills, influenza-like illness, pain, Chest pain Nervous system: Headache, dizziness, Disturbance in attention, migraine, memory impairment. Gastrointestinal: Increased lipase, Nausea, diarrhea, vomiting, Increased lipase, abdominal discomfort, constipation, dyspepsia, dry mouth, gastroesophageal reflux. Dermatologic: Pruritus, rash, Alopecia, dry skin. Psychiatric Insomnia, irritability, Depression, anxiety, agitation, Severe depression was reported, particularly in patients with history of psychiatric illness. Hematologic: Decreased hemoglobin, anemia, neutropenia, decreased neutrophils, decreased lymphocyte count, decreased platelet count and decreased platelets, Pancytopenia. Cardiovascular: bradycardia (including cases requiring pacemaker intervention), Decreased weight Musculoskeletal: Myalgia, arthralgia, increased creatine kinase, back pain, muscle spasms Respiratory: Dyspnea, cough, Nasopharyngitis, exertional dyspnea Hepatic: Increase bilirubin, (greater than 1.5 times ULN).</p>
Daclatasvir	<p>General: Fatigue, asthenia, influenza-like illness, pyrexia, Hot flush, pain, weight decreased. Nervous system: Headache, Dizziness, migraine Dermatologic: Pruritus, rash, dry skin, alopecia Psychiatric: Insomnia, irritability, Depression, anxiety Hematologic: Anemia, neutropenia, Thrombocytopenia, Decreased hemoglobin, eosinophilia Respiratory: Cough, nasopharyngitis, dyspnea, Exertional dyspnea, nasal congestion, upper respiratory tract infection Gastrointestinal: Diarrhea, nausea, Upper abdominal pain, constipation, flatulence, gastroesophageal reflux disease, dry mouth, vomiting, elevated lipase Musculoskeletal: Myalgia, arthralgia Common: Back pain Metabolic: Decreased appetite Cardiovascular: bradycardia heart block, cardiac arrhythmias Hepatic: Increased ALT, increased AST Increased total bilirubin [Ref] Genitourinary: Urinary tract infection Ocular: Common: Dry eye [Ref]</p>
Ledipasvir	<p>Applies to ledipasvir / sofosbuvir: oral tablet General: Fatigue [Ref] Nervous system: Headache Gastrointestinal: Nausea, diarrhea, increased lipase Increased lipase, Lipase elevation was transient and asymptomatic. Psychiatric: Insomnia Hepatic: Increased bilirubin</p>



	Cardiovascular: bradycardia, fatal cardiac arrest, cases requiring pacemaker intervention Musculoskeletal: Increased creatine kinase
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6.3 DRUG TOXICITY

Drug toxicity is the unwanted effect of drugs resulting from administration in excess of the required therapeutic dose, or accumulation of drug in the body due to inefficient absorption, distribution, metabolism or excretion. Drug toxicity can be detected clinically (history and clinical examination) and/or through laboratory testing.

In the event of drug toxicity, the offending drug(s) must be discontinued and changed to another drug from within its class. In adverse drug reactions, the patient should be managed based on the classification of the ADR.

6.3.1 Laboratory Toxicity Monitoring

Laboratory monitoring of patients receiving Pegylated interferon based regimens for hepatitis treatment is very important for early detection and prevention of some ADRs. The abnormal laboratory values (laboratory test abnormalities) may be early warning signals preceding the clinical manifestations of some ADRs in patients receiving anti-hepatitis (medicines). The following laboratory tests are desirable for laboratory toxicity monitoring of patients receiving medicines for treatment or prophylaxis:

The severity grading of laboratory test abnormalities may guide prompt intervention and prevent the negative consequences of ADR. The following guide (Table 15) can be used to estimate the severity grade of laboratory adverse events:

Table 15: Severity Grading of Laboratory Adverse Events in Adults and Adolescents

LABORATORY TEST ABNORMALITIES						
Item	Reference Range	Grade 1 Toxicity	Grade II Toxicity	Grade II I Toxicity	Grade IV Toxicity	
HAEMATOLOGY						
Hemoglobin	10.5 - 18.0g/dl	8.0 - 9.4 g/dl	7.0 - 7.9 g/dl	6.5 - 6.9 g/dl	< 6.5 g/dl	
Absolute neutrophil count or Granulocyte count	2.0 - 7.5 x10 ⁹ /L	1 - 1.5x10 ⁹ /L	0.75 - 0.99x10 ⁹ /L	0.5 - 0.749 x10 ⁹ /L	<0.5 x 10 ⁹ /L	



Platelet count	100–450 x 10 ⁹ /L	70–99x 10 ⁹ /L	50 – 69 x 10 ⁹ /L	30 – 49 x10 ⁹ /L	< 29 x 10 ⁹ /L
Total WBC	4.0 – 11.0x10 ⁹ /L	2.0- 3.9x10 ⁹ / l	1.0 – 1.9 x 10 ⁹ /L	< 1.0 x 10 ⁹ /L	-
CHEMISTRY					
ALT	5.0 – 38U/L	1.25 - 2.5 x ULN	>2.5 – 5xULN	>5.0 –10 x ULN	>10 x ULN
Triglycerides	<1.69 mmol/l	1.69- 2.25 mmol/l	2.26- 5.63mmol/l	5.64- 13.5mmol/ L	>13.56 mmol/L
Cholesterol		>1.0 - 1.3 x ULN	4.52- 8.48mmol/ L	8.49- 13.56mmol /l	>13.56mmol /L
Lactate	< 2 mmol/l	-	2 – 5 mmol/l	5 – 10 mmol/l	>10mmol/ l
Glucose (hyperglycemia)	4 – 6 mmol/l	6 – 8.9 mmol/l	8.91- 13.88mmol /l	13.89- 27.76mmol /l	> 27.76mmol/l
Glucose (hypoglycemia)	4 – 6 mmol/l	3.01- 3.55mmol/l	2.19-3.00 mmol/l	1.67-2.18 mmol/l	<1.67 mmol/l
Amylase	28 – 100U/L	> 1.0– 1.5 x ULN	> 1.5 – 2.0 x ULN	> 2.0 – 5.0 x ULN	> 5.0 x ULN
Bilirubin	2 – 21µmol/L	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	> 5.0 x ULN
Lipase	< 1.5 U/mL	> 1.0– 1.5 x ULN	> 1.5 – 2.0 x ULN	> 2.0 – 5.0 x ULN	> 5.0 x ULN
Creatinine	0.7 – 1.5mg/dl or 62 – 133µmol/ L	> 1.0 -1.5x ULN	> 1.5-3.0 x ULN	> 3.0-6.0 x ULN	> 6.0 x ULN



Sodium Hyponatraemia	136-145 mmol/l	130 - 135mmol/l	123- 129mmol/l	116- 122mmol/l	<116mmol/l
Sodium Hypernatraemia	136- 145mmol/l	146 - 150mmol/l	151- 157mmol/l	158 - 165mmol/l	>165mmol/l
Potassium Hyperkalaemia	3.5 – 5.0 mmol/l	5.1 – 6.0 mmol/l	6.1– 6.5 mmol/l	6.6 - 7.0 mmol/l	>7.0mmol/l
Potassium Hypokalaemia	3.5 -5.0 mmol/l	3.5 -3.0 mmol/l	3.0 -2.5 mmol/l	2.5 -2.0 mmol/l	<2.0mmol/l
Management	Continue Antiviral Therapy, and consult expert		Continue Antiviral Therapy, and consult expert	Consider stopping Antiviral Therapy and consult expert	
Lipid imbalances could be managed with exercise, diet and pharmacologically using fibrates and/or statins					

6.4 STEPS TO RECOGNIZE ADVERSE EVENTS (AES)

- Health care workers should;
- Ask and look for any Aes
- Take a detailed history of the patient
- Establish time relationships; as the time from the start of therapy/immunization to the time of onset of the suspected reaction should be logical
- Carry out a thorough physical examination with appropriate laboratory investigations (if necessary)
- Check the known pharmacology of the medicine, intervention or medication given

6.5 PRINCIPLES OF MANAGEMENT OF ADVERSE DRUG REACTIONS AND ADVERSE EVENT FOLLOWING IMMUNIZATION

Ensure routine screening of all patients receiving medicines for signs/symptoms indicating possible AE using the appropriate forms (see Appendix I and II).

- If there are no new signs and/or symptoms indicating possible adverse reactions, continue case management of patients.
- If there are any new signs and/or symptoms indicating possible adverse reactions:
 - Determine the severity of the adverse event(s) using WHO Severity Grading of ADRs
 - If the suspected adverse event(s) is mild (ADR severity grade 1), counsel patients on how to manage the adverse event(s), document intervention and then manage patients as appropriate.

If the suspected adverse event(s) is moderate, severe or life-threatening (ADR severity grade II –



IV), manage the patients' AEs as appropriate and then document intervention, report the adverse events using the Yellow Form and Adverse Event following Immunization Reporting Form.

What Should Be Reported About ADRs?

- All suspected reactions/incidence that occurred after administration of new medicines
- All serious or unexpected (unusual) AEs that one suspects for established or well-known drugs
- If an increased frequency of a given reaction is observed
- All suspected AEs associated with drug-drug, drug-food or drug-food supplement interactions.
- ADRs in special fields of interest such as drug abuse, misuse, medication error, overdose, occupational exposure, pregnancy, breastfeeding mothers and the aged population.
- ADRs related to failure of contraceptives
- Lack of efficacy of a medication, or when suspected pharmaceutical defects are observed
- Reactions suspected of causing death, danger to life, hospital admissions, prolonged hospitalization, or birth defects.
- When in doubt whether the suspected adverse event/reaction is an ADR or not, you must report to the National Pharmacovigilance Centre.
- Only complete ICSRs and AEFI reports should be transmitted to the NPC.
- Components of complete ICSR include identifiable patient, identifiable reporter, event and the drug

All ADRs should be reported on time (refer to guidelines and policy) to the National Pharmacovigilance Centre using the Yellow form approved by the National Agency for food and Drug Administration and control (NAFDAC). Channels for reporting include;

- Health Institutions (PHC, SHC, THC as well as private hospitals)
- NAFDAC State Pharmacovigilance offices
- Zonal Pharmacovigilance office
- NAFDAC headquarters
- PRASCO (Pharmacovigilance Rapid Alert System for Consumer Reporting
- Food and Drug Services Department), FMOH
- All AEFI during routine immunization within 30 days and up to 42 days for mass campaigns.

Antiviral (anti-hepatitis) drugs must be stopped immediately if there is suspected life threatening adverse drug reaction (grade IV) following the provisions of the national guidelines.

When dealing with multiple drugs suspected to be associated with an ADR, consider the possibility of a drug-drug interaction. Furthermore, do a label and literature search (consult the NPC and drug information focal person as necessary).

Establish a functional hospital – based pharmacovigilance committee (with a term of reference) in all centers to coordinate medicines clinical pharmacovigilance; refer all cases of AEs to the hospital based PV committee.



6.6 DRUG-DRUG INTERACTIONS

Drug interaction is the modification of the mechanism of action of one drug by another. Drug interactions can be beneficial, of no consequence, or harmful. Multiple drug use ('polypharmacy') is extremely common in patients being managed for CHB and CHC, so the potential for drug-drug interaction is likely. Adverse drug interactions can be catastrophic, but are often avoidable.

It is important to note that Anti-viral drugs are metabolized by the Cytochrome P450 3A4 isoenzyme in the liver. As a result, other drugs metabolized by this enzyme can either raise or lower the level of antivirals or be increased or decreased themselves by these interactions.

Table 16. Drug-Drug Interactions between co-administered HIV and HCV treatment

HIV Antiviral Drugs	Sofosbuvir	Daclatasvir	Ledipasvir /Sofosbuvir	Pegylated IFN	Ribavarin
<i>NRTIs</i>					
Abacavir (ABC)	◆	◆	◆	■	■
Lamivudine (3TC)	◆	◆	◆	■	●
Zidovudine (AZT)	◆	◆	◆	●	●
Tenofovir	◆	■	■	■	■
<i>NNRTIs</i>					
Efavirenz (EFV)	◆	■	■	◆	◆
Nevirapine (NVP)	◆	■	◆	◆	◆
<i>Protease Inhibitors</i>					
Atazanavir (ATV/r)				◆	■
Lopinavir	◆	◆	◆	◆	◆
Ritonavir	◆	■	◆	◆	◆

● These drugs should not be co-administered

■ Potential interaction

◆ No clinical significant interaction expected

6.7 PREVENTION OF ADVERSE DRUG REACTIONS

- Applying the principles of rational use of medicines can prevent most ADRs:
- Use of few drugs, whenever possible
- Use drugs that you are familiar with
- Do not change therapy from known drugs to unfamiliar ones without good reason
- All patients commencing medicines should be properly counseled on the ADRs related to the medications and what to do when it occurs or is suspected. The healthcare provider should be knowledgeable about this
- Be vigilant (look for) these adverse effects when initiating therapy and during follow-up visit



CHAPTER SEVEN

PROGRAMMATIC MANAGEMENT OF VIRAL HEPATITIS

The successful implementation of the recommendations in these guidelines and establishment of affordable prevention, treatment and care programs for viral Hepatitis in the public and private sectors will depend on a well-planned process of adaptation and integration into relevant national strategies. Essential operational and service delivery issues will be addressed on an ongoing basis to ensure long-term effectiveness and sustainability of the national Program. This will be achieved by making the best use of available human and financial resources, thereby maximizing retention of patients across the continuum of care. Specifically, efforts will be made to promote task shifting, improve laboratory and diagnostic services; and strengthen procurement and supply management systems.

7.1 DECENTRALIZATION AND INTEGRATION OF SERVICES

Viral hepatitis treatment and care services providers should implement recommendations from this National Guidelines for the decentralization of Treatment Centers. Decentralization and integration of Viral Hepatitis services will contribute to improvement in the accessibility and ownership of services.

Under this arrangement PHCs can offer prevention services such as screening, vaccination, PMTCT and referrals. Trained clinicians can perform treatment initiation.

The key programmatic components of service delivery for Viral Hepatitis care and treatment are adequate clinic infrastructure, human resources, Health Care Workers (HCWs), a referral system, laboratory and diagnostic services, reliable drug supply, monitoring and evaluation, civil society engagement and private sector participation.

7.2 HUMAN RESOURCE DEVELOPMENT

The limited availability of skilled health workers to deliver quality services is a major setback to the attainment of universal access to viral hepatitis prevention, treatment and care. At all levels of service provision, whether at health facility or community-based there should be adequate human resource to cater for the needs of patients. However, this is not the case and as such several interventions should implemented be to boost human resource for Viral Hepatitis.

7.2.1 Training of Health Workers

All health workers involved in the provision of Viral Hepatitis services must have received adequate training prior to offering services and re-trained thereafter.

Training of health workers must conform with globally accepted standards using nationally approved viral Hepatitis training curriculum and manuals



7.2.2 Training of Community Members

Community volunteers should be trained to provide sensitization and mobilization services for viral hepatitis control, using a community directed intervention approach.

7.2.3 Personnel Recruitment and Retention

Governments, agencies and stakeholders at all levels of care should ensure availability of adequate numbers of health workers at all facilities providing viral Hepatitis services.

7.2.4 Task Shifting

Government and implementing agencies at all levels should adopt task-shifting strategies, which involves the rational redistribution of tasks among health workforce teams. It involves health workers undertaking tasks that are not listed in their professional schedule of duties. Task shifting reduces the burden of work on a particular cadre of health worker and increases the efficiency and productivity in health facilities with large volumes of patient. Task shifting applies to the different services that are offered to the community.

7.3 PROCUREMENT AND SUPPLY MANAGEMENT SYSTEMS

Procurement and supply management systems are required to ensure that viral hepatitis commodities, including antiviral medicines, vaccines and laboratory commodities are available in sufficient quantities at all times when they are needed. This depends on adequate financing, forecasting, supply planning, procurement, warehousing, distribution and tracking. The successful administration of this system requires multi-team collaboration including pharmacists, medical officers, medical records personnel, procurement officers, distribution agents, customs and excise officers, shipping agents, manufacturers of the commodities and administrators of health facilities. The very first step is in determining what should be procured and in what quantity.

Drugs and other commodities required for viral hepatitis prevention treatment and care include:

- Vaccines
- Anti-viral drugs
- Rapid test kits and consumables
- Viral load reagents, sample collection kits, and consumables
- Equipment, reagents and consumables for haematology and chemistry laboratory tests

7.3.1 Viral Hepatitis commodities, Storage and Distribution

The commodity distribution process begins when requests are made, processed and the commodities get to the end user through health care providers at service delivery point.

The logistic system for viral hepatitis is aligned with the existing harmonized Logistics Management Information System. The responsibility for maintaining appropriate stock levels rests on the facility logistics team. Facility's replenishment for consumed stock occurs bi-monthly in response to submission of copies of the ordering Combined Report and Request forms. The reports are directly transmitted to the Central Medical Stores and then to the Logistics Unit in the National Programme where they are analysed for various decisions – ranging from routine re-supply to quantification and forecasting and supply planning. Feedback on reports from the facilities is processed by the Logistics Unit of NASCP and communicated to the facilities. When orders are ready for pick-up, distribution agents are notified and the commodities are transported



and delivered directly to the service delivery points.

Table 7.1: National Reporting schedule

Bimonthly Review Period	Report sent to the central
January – February Report	1st – 7th March
March – April Report	1st – 7th May
May – June Report	1st – 7th July
July – August Report	1st – 7th September
September – October Report	1st – 7th November
November – December Report	1st – 7th January

7.3.2 Key features of Nigerian Viral Hepatitis commodities' logistics system

Inventory Control System

The forced ordering (“Pull” system) has two-levels (Central and Facility) and is based on maximum-minimum thresholds. Service delivery points are “forced” to order at the end of the review period (2 months in FMOH program).

The quantity of commodities in the logistics system is tracked as a stock status (i.e. how long stocks will last).

The maximum stock level (4 months of stock in FMOH program) is set high enough to guarantee adequate supply at all times during the ordering cycle, but low enough to prevent overstock and wastage.

The minimum stock level (2 months of stock in FMOH program) is set as low as possible but includes a safety margin to prevent stock-outs.

The stock level in the facility has to be assessed frequently as this will alert the storekeeper in case of the need to place emergency order. The emergency order is done when stock levels drop to 2 weeks of stock; it disregards the review period. The quantity to order is calculated to top up the stock on hand to maximum level.

7.3.3 Logistics Management Information system (LMIS)

One of the primary components of any logistics system is a functional Logistics Management Information System (LMIS) that ensures availability of timely and accurate data for decision-making. These essential data must always be collected for products at all levels.

The three essential data elements include;

Stock on Hand: Describes the quantities of usable stock of commodities available at a particular point in time. Stock-on-hand information guides us when to place an order and how much of each item is in stock. It also guides redistribution decisions.

Consumption: Describes the quantity of commodities used during the report and order cycle. The rate of consumption is the link between the consumer and the supply chain.

Losses and Adjustments: Losses include the quantity of commodities removed from the distribution system for any reason other than usage (e.g. losses, expiry, and damage). Adjustments may include receipt or issue of supplies to or from one facility to another that is not



their usual supplier (e.g. a transfer) or a correction to account for a difference between what was counted during a physical inventory and what was recorded on the inventory control card. Losses/adjustments may therefore be a negative or positive number.

In order to collect and report the above mentioned data items, a number of forms described below were designed for the management of these commodities.

7.3.4 The LMIS Forms /Tools

Inventory Control Card

This tracks the quantity of health commodities (vaccines, anti-viral drugs, etc) in a facility's storage area. This record collects two essential data items: stock on hand and the losses & adjustment data. The Inventory Control Card should always be kept in a facility's storage area.

Daily Consumption Record for Vaccines, Anti-Viral drugs and Daily Usage Record or Register for Test Kits and Reagents

These collect the number of commodities that have been used in the facility daily over a defined period of time. This information is called Consumption data and is one of the essential data items. The Daily Consumption Record for Anti-Viral drugs should be kept with the person(s) who dispenses. The Daily Usage Record for test kits and reagents should be kept with the person(s) who runs the lab tests.

Record for Returning/Transferring Commodities

This is a transactional form that is used in the event that commodities may be required to be returned to the CMS or transferred to another facility at the same level for various reasons ranging from expiry, damage, change in the treatment guidelines, or over-stocking.

Combined Report Requisition Issue and Receipt Form (CRRIRF)

This form summarizes the information that is collected on the Inventory Control Card, Daily Consumption Record, and Daily Usage Record and is sent to the central store on a regular basis. The CRRIRF uses this reported data to calculate the facility order quantities and monitor whether stock is maintained according to plan (no overstock, shortages, or stock outs). Information from this report is critical to a well-functioning logistics system.

Roles and Responsibilities of Logistics personnel

Central Store Pharmacist

- Receives commodities
- Fulfils orders (re-supply)
- Updates Inventory Control Card when commodities are issued or received
- Ensures the storage of commodities according to the storage standards
- Helps to manage commodities in the warehouse
- Generates national-level reports

Central Store Officer

- Ensures the storage of commodities according to the storage standards
- Updates inventory control cards



Facility Pharmacists/Laboratory Scientist

- Completes the daily consumption record and usage record for commodities Documents all transactions in the inventory control cards maintained in the unit
- Orders commodities and issue commodities to the various points of service in the facility
- Completes the CRRIRF at the end of review period
- Collects the daily consumption and usage registers / reports from other locations where commodities are dispensed e.g. PMTCT units and feeder sites
- Sends back unusable commodities that must be returned to the CMS after filling out the record for returning commodities
- Aggregates all usage data from the daily usage register for commodities and enter in the Combined Reports Requisition Issue and Issue Forms and send to the Central Warehouse
- Monitors the management of commodities in the store.

Facility Anti-Viral Team Leader

- Endorses CRRIRF to be sent to the central store

7.4 MONITORING AND EVALUATION

7.4.1 Monitoring implications

Monitoring and evaluation will help programme managers assess the effectiveness of interventions and linkages between services along the cascade of prevention, treatment and care for Hepatitis and related conditions (Fig 7.1). This information is essential to detect and respond to challenges or gaps in programme performance and quality of services. As the programme matures, monitoring individual and population level outcomes, including toxicity and adverse events, drug resistance, viral suppression, mortality, survival and incidence, is also essential to assess its impact.

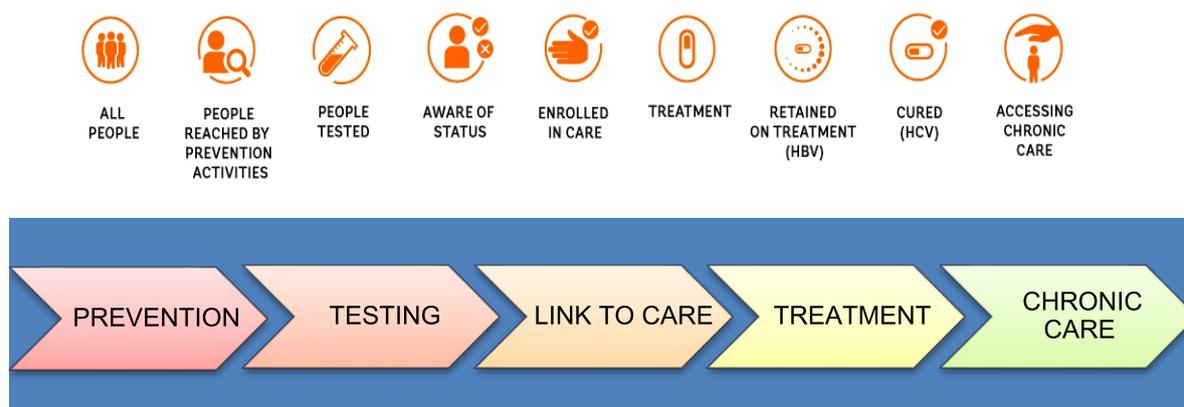


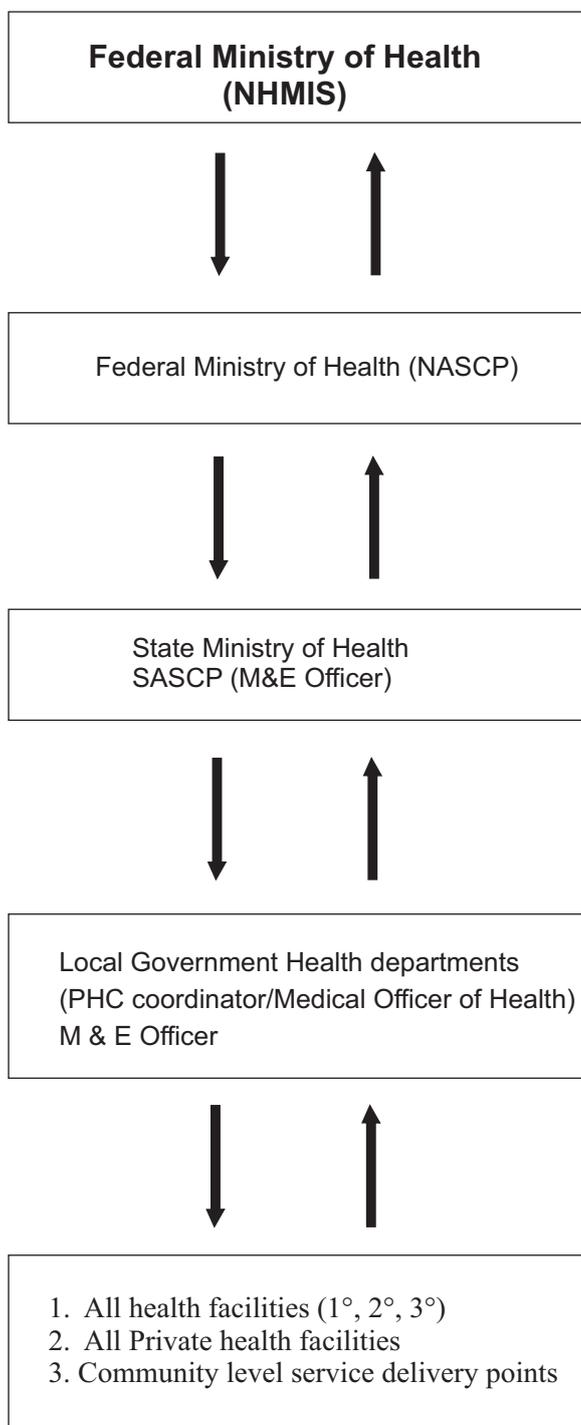
Fig7.1 Viral Hepatitis prevention, treatment and care cascade



7.4.2 National framework for results-based management

The National framework for results based management will enhance the effective monitoring of strategies and activities towards an effective monitoring of the hepatitis response in Nigeria.

Fig7.2: Data flow process



Collection of data will be done through routinely reported data from all facilities or sentinel sites; population-based surveys; surveillance data; observations on cohorts of people living with Hepatitis; and periodic evaluation.

Programme input and processes can also be monitored through facility surveys or updated lists of service availability including documenting the availability and training of human resources and monitoring the availability of Hepatitis medicines and diagnostics at various geographical and service delivery points.

Special studies can be considered to support routine monitoring. In considering how best to collect critical data, efforts should also be made to review monitoring systems, such as better linkage of the monitoring of Hepatitis with HIV, TB and other disease conditions both at the community and facility levels.

7.4.3 Monitoring and Evaluation guidelines for Viral Hepatitis Control Program in Nigeria for State and LGA Health Workers

A guideline focusing on national core indicators, tools and methodology for monitoring and evaluation of viral hepatitis in Nigeria has been developed. All states and LGAs in Nigeria are expected to collect and use the minimum core indicators as enunciated in the National Health Sector M & E guidelines.

Objective: To provide orientation on viral hepatitis monitoring & evaluation.

Expected Outcome: Users to appreciate the critical role of Monitoring and Evaluation in the implementation of viral hepatitis in Nigeria in order to achieve the strategic targets.

Monitoring: This is a process of tracking the progress and identify challenges of the implementation of planned activities and their outputs (using process/output indicators). This will ensure that activities are carried out in a timely manner, implemented according to planned objectives, ensure judicious use of resources and entrench accountability.

Evaluation: This is a process of measuring **Outcomes** and **Impacts** of interventions. Evaluation of outcomes and impacts is needed to document periodically whether defined strategies and implemented activities leads to expected results in terms of:

- **Outcomes:** e.g. cure rate for HCV, rate of coverage of vaccines etc.
- **Impacts:** e.g. reduction of morbidity, mortality or economic losses.

7.4.4 Monitoring the outputs and outcomes of scaling up access to antiviral drugs

In addition to monitoring the implementation of the strategies, Health Information Systems will also monitor the outputs and outcomes associated with the interventions. Table 7.1 lists areas for gathering data for assessing programmes that lead to anticipated outputs and outcomes at various points along the cascade of hepatitis treatment and care.



Table 7.1: Overview of data areas for monitoring and evaluating the hepatitis treatment cascade

Step in the cascade for care	Indicator areas	Relevance
Epidemic Pattern	Number of people living with hepatitis in various categories	Estimates the prevalence and distribution of people living with hepatitis among the population. Estimates the size of relevant populations and need for hepatitis interventions, to reflect service needs and focus planning
Prevention	Hepatitis B vaccination: new-borns, infants, adults	This indicator monitors and guides immunization programmes to prevent MTCT of HBV
Testing	People diagnosed	Number of people newly diagnosed estimates the proportion of persons with hepatitis who know their status and measures the entry point to the continuum of care, disaggregated estimates can point to gaps in diagnosing people chronically infected with viral hepatitis
Care and Treatment	Treatment coverage/initiation	Measures strength of link between diagnosis and enrolment in care. Indicates access to treatment. Trends over time reflect on progress in treating patients.
Cure	Cure (HCV) or Viral suppression (HBV)	Measures how many are cured among those who completed treatment (HCV), Measures virological suppression achieved among all those currently on treatment regardless of when they started



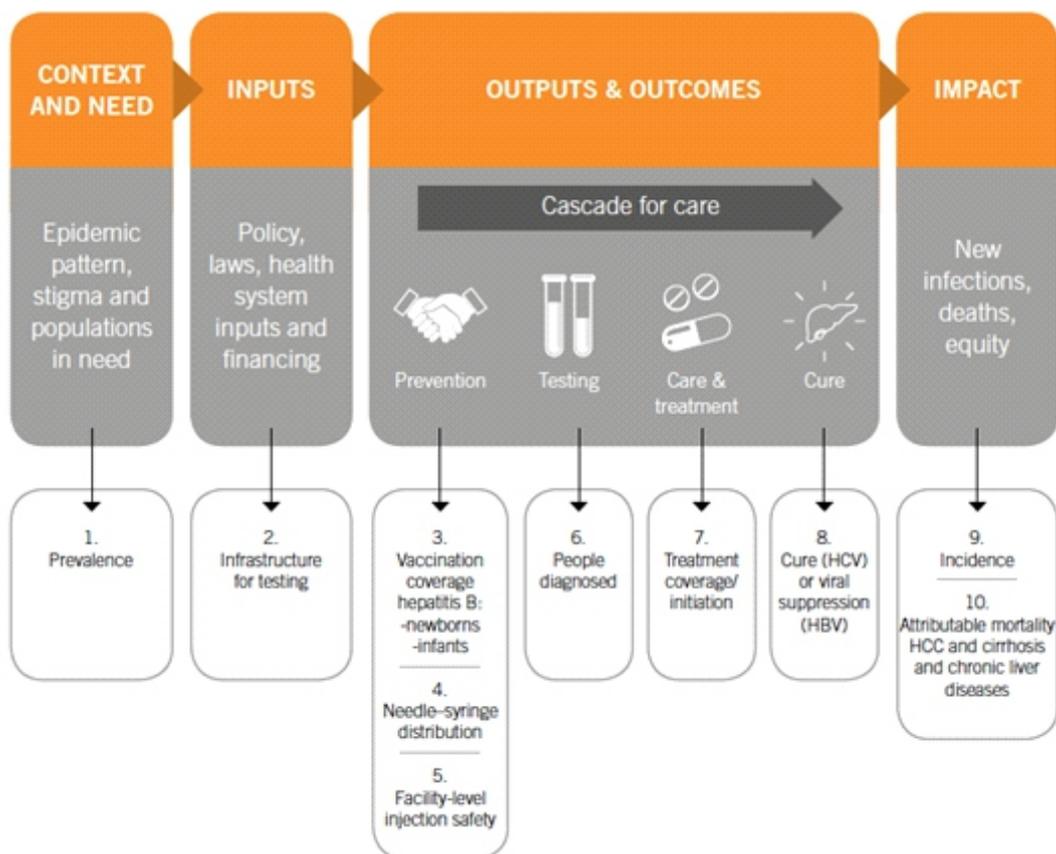
Table 7.3: Monitoring of the key interventions

Summary of new recommendation areas	Implications for monitoring	Responsible groups
Awareness creation	Data on percentage coverage; number of persons aware of status	NASCP
Viral Hepatitis testing and counselling	Data on percentage coverage; number of persons tested	NASCP
HBV/HCV/HIV testing and counselling	Data on Hepatitis B and C among people in HIV care	NASCP
Persons in care	Data on the number and percentage of different populations (such as adults, adolescents, children and pregnant and breastfeeding women) who are in care based on the eligibility criteria Review of the monitoring system for assessment is needed and how best to collect the relevant data, disaggregated by age and sex	
Persons on treatment including co-morbidities	Data on the antiviral regimen among different population such as adults, adolescents, children, pregnant and breastfeeding women. Monitoring tools may need to be adjusted to reflect regimen options. Monitoring on virologic cure after 12 weeks of treatment for HCV patients Monitoring of the antiviral regimens for the HIV/HBV/HCV co-infected individuals	
Response to treatment and diagnosing treatment failure	Data on percentage of people receiving treatment that had a viral suppression and /or SVR	
Service delivery	Data on retention and adherence among various populations Monitoring of the integration of Hepatitis into facilities providing HIV services, maternal and child health services, STI services and drug dependence services Monitoring the functionality of linkages from HIV, maternal and child health, STI and drug dependence services to hepatitis care and linkages between communities, transfers peripheral facilities and hospitals	
Task shifting	Data on the number of non-physician clinicians, midwives and nurses who are trained in the management of Hepatitis. Monitoring of the number of community health workers who are trained on the management of Hepatitis	



APPENDIX 1

Monitoring and Evaluation Framework: 10 indicators to measure the health sector response





**NATIONAL AIDS/STIS CONTROL PROGRAM
FEDERAL MINISTRY OF HEALTH
2016**