

Republic of Rwanda



Ministry of Health

NATIONAL GUIDELINES FOR THE PREVENTION AND MANAGEMENT OF VIRAL HEPATITIS B AND C

June 2015



FOREWORD

Viral Hepatitis, caused by the hepatitis B virus (HBV) and hepatitis C virus (HCV) are characterized by the inflammation of liver cells, and may cause hepatocellular carcinoma (HCC) and cirrhosis if not treated. HBV and HCV infections can be either acute or chronic, and their associated illnesses range in severity from asymptomatic to symptomatic progressive disease stages. Chronic hepatitis B (CHB) and chronic hepatitis C (CHC) are major public health problems. According to recent WHO statistics (2015), worldwide, there are an estimated 240 million HBV chronically infected people, particularly in low and middle income countries. Between 20% and 30% of those who become chronically infected will develop these complications, and an estimated 650 000 people will die annually due to CHB related complications.¹

More than 185 million people around the world have been infected with HCV since 2005, and each year 350 000 die due to CHC related complications.²

The majority of people are unaware of their HBV or their HCV infection status. For those who have been diagnosed, treatment remains inaccessible and with the current HIV pandemic, viral hepatitis and HIV co-infection remain a critical disease burden.

In terms of HBV prevention, universal HBV immunization programs that target new born infants, with the first dose at birth, have been highly effective in reducing the incidence and prevalence of hepatitis B in many endemic countries.

Additionally, antiviral agents active against HBV are available, and have been shown to suppress HBV replication, prevent progression to cirrhosis, and reduce the risk of HCC and liver-related deaths. However, currently available treatments fail to eradicate the virus in most treated cases, necessitating potentially lifelong treatment.¹

Hepatitis C infection differs from hepatitis B infection as it can now be cured using antiviral active treatments. Several medicines are available to treat people infected with HCV, and cure rates have steadily improved with the introduction of newer medicines since 2012.³ These new medications can

cure more than 90% of people with HCV infection and are effective against genotypes that were previously difficult to treat.

The 2015 edition of the National Guidelines for the prevention and management of Viral Hepatitis B and C were developed in line with the recently published WHO guidelines. The current guidelines thus respond to the Ministry of Health's need to improve skills of health care providers as well as the quality of care and treatment offered in both public and private health facilities countrywide, hence contributing to the improvement of the quality of life of HBV and HCV infected people.

The review of the current guidelines would not have been finalized without the esteemed support of all the stakeholders who are involved in the domain of HIV-AIDS and other blood borne infections control in Rwanda.

We give our sincere thanks and appreciation to the members of the hepatitis technical working group and respective organizations that contributed to the development of this document.

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LIST OF ACRONYMS AND ABBREVIATIONS

AFP	Alpha Feto-Protein
AIDS	Acquired Immuno Deficiency Syndrome
ALT	Alanine aminotransferase
Anti-HBe	Antibody to Hepatitis B e antigen
Anti-HBs	Antibody to the Hepatitis B surface antigen
Anti-HCV	Antibody to the Hepatitis C Virus
APRI	Aminotransferase to Platelet Ratio Index
ART	Antiretroviral Therapy
ASSIST	Alcohol Smoking and Substance Involvement Screening Test
AST	Aspartate aminotransferase
AUDIT	Alcohol Use Disorders Identification Test
CD4	Cluster of Differentiation 4
CHB	Chronic Hepatitis B
CHC	Chronic Hepatitis C
CLD	Chronic Liver Disease
CrCl	Creatinine Clearance
DCV	Daclatasvir
DNA	Deoxyribonucleic acid
ELISA	Enzyme-Linked Immuno Sorbent Assay
GFR	Glomerular Filtration Rate
Hb	Hemoglobin
HBeAg	Hepatitis B Virus Early Antigen
HBIG	Hepatitis B Immune globulin
HBs Ag	Hepatitis B surface Antigen
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma

HCV	Hepatitis C Virus
HCWs	Community Health Workers
HIV	Human immunodeficiency virus
IFN	Interferon
IVDU	Intravenous Drug Users
LDV	Ledipasvir
MSM	Male having sex with men
NAT	Nucleic Acid Amplification Technology
PCR	Polymerase Chain Reaction
PWID	Persons Who Inject Drugs
RBV	Ribavirin
RNA	Ribonucleic Acid
RT-PCR	Reverse Transcription Polymerase Chain Reaction
RVR	Rapid Virological Response
SOF	Sofosbuvir
STIs	Sexually Transmitted Infections
SVR	Sustained Virological Response
TDF	Tenofovir Disoproxil Fumarate
VL	Viral Load
WHO	World Health Organization

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PART I:

HEPATITIS B MANAGEMENT

Chapter I: Overview on Hepatitis B

1.1. Definitions

Hepatitis B Virus Infection: Inflammation of the liver caused by the hepatitis B virus. It can present into acute or chronic form depending on the duration of the infection.

Acute HBV Infection: Presence of HBsAg within six months of acquiring infection. Recovery is accompanied by clearance of HBsAg with seroconversion to anti-HBs (antibodies to hepatitis B surface antigen), usually within 3 to 6 months.

Chronic HBV Infection: Defined as persistence of hepatitis B surface antigen (HBs Ag) for 6 months or more after acute infection with HBV. Over time, the chronic infection can cause liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC).

Immune-tolerant Phase: High replicative phase of infection seen in the early stage of CHB among people infected at birth or in early childhood.

Immune-active Phase: Phase of hepatitis B e antigen (HBeAg)-positive disease characterized by fluctuating aminotransferases and high HBV DNA concentrations. May result in seroconversion from HBeAg to anti-HBe (antibody to hepatitis B e antigen).⁴

Inactive phase (or immune-control phase): Low replicative phase of chronic hepatitis B characterized by HBeAg negativity, anti-HBe positivity, normal alanine aminotransferase (ALT) and HBV DNA concentration below 2000 IU/mL.⁵

HBeAg seroconversion: Loss of HBeAg and seroconversion to anti-HBe.

HBsAg seroconversion: Loss of HBsAg and development of anti-HBs.

HBeAg reversion: Reappearance of HBeAg in a person who was previously HBeAg negative and usually associated with increased HBV replication.⁶

Cirrhosis: An advanced stage of liver disease characterized by extensive hepatic fibrosis, nodularity of the liver, alteration of liver architecture and disrupted hepatic circulation.

Decompensated cirrhosis: Clinical complications of cirrhosis become manifest, including jaundice, ascites, spontaneous bacterial peritonitis, esophageal varices and bleeding, hepatic encephalopathy, sepsis and renal failure.⁷

Hepatocellular carcinoma (HCC): Primary cancer of the liver arising in hepatocytes.

1.2. Transmission of HBV

HBV shares the same mode of transmission as HIV:

- Blood and biological fluids contact (including needle stick injury)
- Unsafe blood transfusion and blood product transfusion
- Unprotected sexual contact (heterosexual and homosexual)
- Vertical transmission (mother to child): perinatal transmission (at the time of, or shortly after birth, and rarely in the second or third trimester of pregnancy)
- Horizontal transmission: household contact, intra-familial, child-to-child
- Shared syringe use (for health facilities or intravenous drug users)
- Other unhygienic medical practice, for examples lasers, inadequate sterilization (razors, dental and surgical procedures)
- Unhygienic practice of non-medical risk associated activities including but not limited to manicures, tattoos, toothbrush sharing, traditional surgical and scarification practice and hair salons

1.3. Groups at High Risk of Hepatitis B Infection

- Pregnant women
- Individuals infected with HIV or HCV
- Health care workers exposed to biological fluids
- People who ever received blood or blood products
- Inmates of correctional facilities
- Household and sexual contacts of HBsAg positive people
- Sex workers
- Male having sex with men (MSM)
- Persons needing immunosuppressive therapy
- Persons who have ever injected drugs
- Children born to HBV positive mothers
- History multiple sexual partners or STIs
- Patients undergoing renal dialysis

Chapter II: Hepatitis B Prevention

Most people who are infected with HBV are unaware of their chronic infection. They are at high risk of developing severe chronic liver disease and can unknowingly transmit the infection to other people.⁸

The prevention of hepatitis B infection consists of primary, secondary and tertiary prevention.

2.1. Primary Prevention of Hepatitis B Infection

The primary prevention of hepatitis B infection consists of activities aimed at reducing or eliminating potential risk for HBV transmission such as increasing awareness and knowledge of the general and high risk population on HBV transmission and prevention.

The following are specific areas of HBV primary prevention strategies:

2.1.1. Communication for Behavior Change

- Increased awareness and knowledge of HBV transmission and prevention and control of the general population
- Provide specific message to increase awareness and knowledge of HBV transmission and prevention and control in the high risk groups
- Training of health care providers

2.1.2. Infection Control Precautions in Community Settings

- Harm reduction practices for injecting drug users prevent HBV transmission
- Safe injections for IVDU

- Avoid unsafe practices around non-medical or traditional practice (cosmetic, scarification, tattoos, circumcision procedures, traditional medical practice)
- Safe household practice (handling or sharing of sharp objects, sharing toothbrushes, hand washing, safe blood contact, avoid intimate contact with carriers)
- Promotion of correct and consistent condom use
- Avoid multiple partners, seek regular screening and treatment for STIs
- Routine screening of sex workers for catch-up HBV immunization
- Vaccination of HBs Ag negative sexual partners of persons with CHB
- Integrated action to eliminate discrimination and gender violence, and to increase access to medical and social services for vulnerable persons

2.1.3. Prevention of HBV Infection in Health-care Settings

Occupational safety measures to prevent transmission of viral hepatitis to health care workers through:

- Hand hygiene including surgical hand preparation, hand washing and use of gloves
- Safe handling and disposal of sharps and waste
- Safe cleaning of equipment
- Testing of donated blood and blood products
- Improved access to safe blood and blood products
- Training of health personnel
- Follow standard universal precautions with open cuts or bleeding
- Safe injections in medical facilities
- Screening of the general population for HBV
- Management of HBV infected patients including health care providers

2.1.4. HBV Vaccination of All Non-Immune People

A. Routine Birth Dose Vaccination against HBV

Consists of a monovalent vaccination dose of all newborn babies within 24 hours of birth followed by three doses (administered as part of the pentavalent dose program). In the case a pregnant mother is known to be HBsAg positive and has a high HBV viral load peri-partum, HBIG (within 14 days) could be recommended in conjunction with birth dose vaccination⁹ (Refer to table 1).

B. Routine Adult Vaccination against HBV

HBV vaccination is recommended to all HBV non-immune people (unvaccinated or non-exposed).

Table 1: Hepatitis B Vaccination Schedule in Rwanda

Hepatitis B Vaccination Schedule Recommended in Rwanda					
N°	Group	Dose 1	Dose 2	Dose 3	Dose 4
1	Newborn	< 24 Hours	Week 6	Week 10	Week 14
2	Adult	Mo	M1	M6	NA
2	HIV+ Adult	Mo	M1	M2	M6

Note:

- It is recommended to vaccinate all babies within 24 hours after birth
- Whenever possible, we recommend to test anti-HBs 2 months after the last dose of vaccination to check if the patient is protected (> 10 IU/L)
- It is advised to get screened for HBsAg and Anti-HBs (Optional) prior vaccination.
- The dosage for adult is 1ml and 0.5ml for newborns
- The dose is doubled (2 ml) in adult HIV-positive people

2.1.5. HBV Post-exposure Prophylaxis

A- General measures

After exposure to blood or other body fluids, the following is recommended as soon as possible:

- Wash the wound site with soap and water;
- If eyes are contaminated then rinse them, while they are open, gently but thoroughly with water or normal saline;
- If blood or other body substances get in the mouth, spit them out and then rinse the mouth with water several times;
- If clothing is contaminated remove clothing and shower with soap;
- Where water is not available use of a non-water cleanser or antiseptic should replace the use of soap and water for washing cuts or punctures of the skin or intact skin.

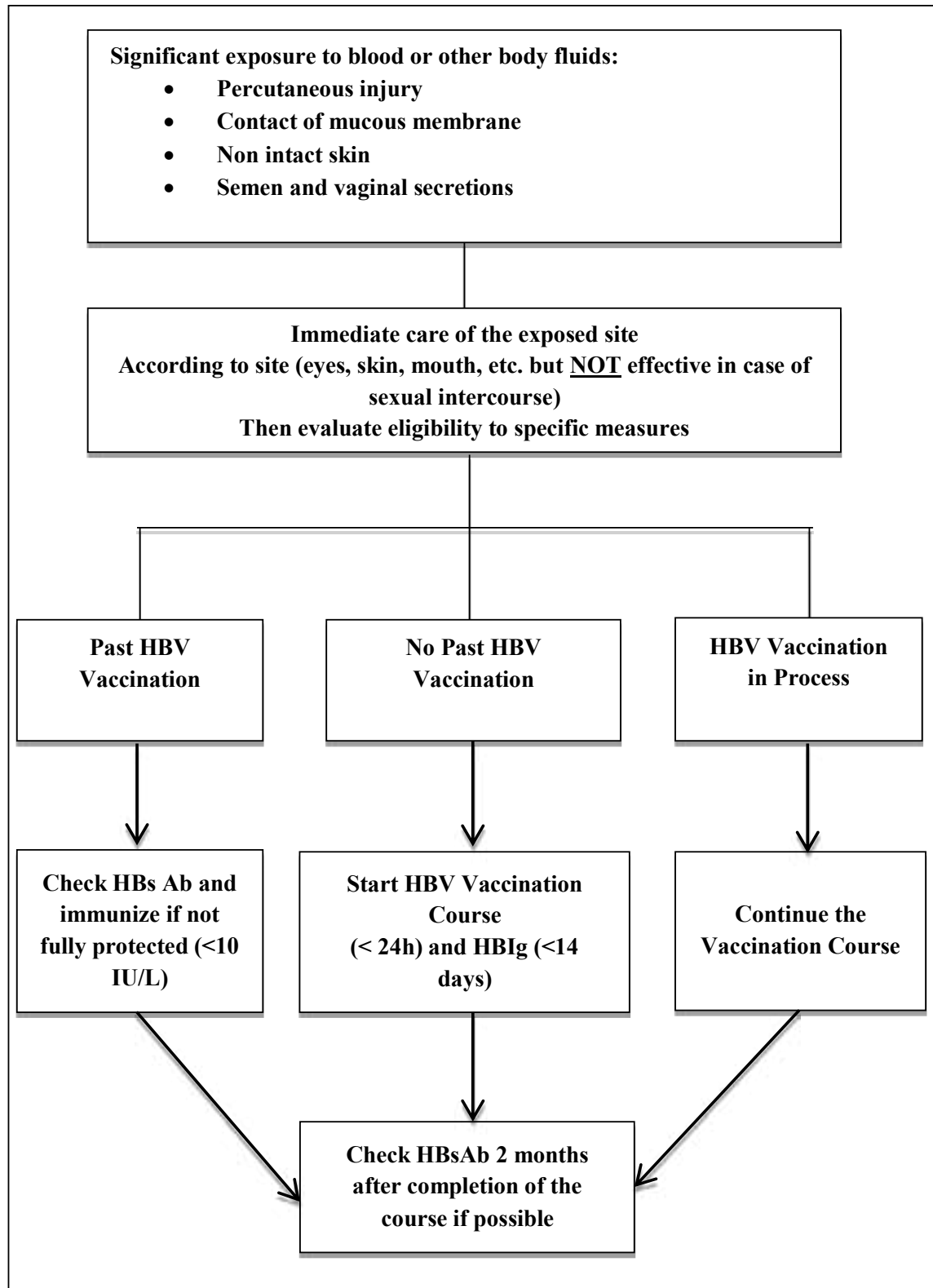
B- Specific Measures

HBV exposure management depends on the following:

- The HBV immuno-status of the exposed person
- Level of the exposed person protection (fully or partially immunized and/or immune)
- Note that both HBIg and first dose of HBV vaccination series should ideally be administered within 24 hours of exposure; HBIg should not be given later than 14 days post exposure but in case HBIg is not available, the active immunization (HBV vaccine alone) is recommended (Fig. 1).

NB: Percutaneous, mucous membrane or cutaneous exposure to (non-blood stained) urine or saliva does not require further assessment, clinical follow up or immunization.

Figure 1: HBV Post Exposure Prophylaxis



2.2. Secondary and Tertiary Prevention of HBV Infection

This prevention aims at early detection of HBV infection for timely treatment and follow up before any advanced liver disease but also reduces HBV transmission.

The early diagnosis helps infected people to take precautions to protect the liver from additional harm by abstaining from alcohol and tobacco consumption, avoiding certain toxic drugs and adopting appropriate diet⁸.

It is therefore advised to screen asymptomatic individuals with focus on high risk groups to provide appropriate counseling and close follow up to those who screen HBsAg positive.

Chapter III: Screening and Diagnosis of Hepatitis B Infection

3.1. Diagnosis Hepatitis B Infection

Hepatitis B is a silent disease since about 50% of people with acute hepatitis B infection are asymptomatic.⁸

Acute infection may cause nonspecific symptoms and clinical signs, such as:

- Jaundice
- Weakness
- Fatigue
- Malaise
- Anorexia
- Nausea
- Vomiting
- Myalgia
- Arthralgia
- Abdominal pain
- Hepatomegaly
- Splenomegaly
- Dark urine
- Low-grade fever

Approximately 5 percent of adults acutely infected with HBV progress to chronic infection and stay in preclinical phase for decades.¹⁰

Therefore, the recommended diagnosis of HBV infection is the evaluation of the patient's blood for hepatitis B surface antigen (HBsAg).

- The presence of HBsAg confirms the infection (acute or chronic)
- The chronic infection is defined as persistence of HBsAg for six months or more after acute infection with HBV
- The presence of HBsAg in HIV-positive will confirm the chronicity of the infection and therefore, there is no need to confirm after six months

3.2. Interpretation of HBV Serologic Markers

Table 2: Interpretation of Hepatitis B Serologic Test Results

Tests	Results	Interpretation
HBsAg	Negative	Susceptible to infection
Anti-HBc	Negative	
Anti-HBs	Negative	
HBsAg	Negative	Immune due to natural infection
Anti-HBc	Positive	
Anti-HBs	Positive	
HBsAg	Negative	Immune due to Hepatitis B vaccination
Anti-HBc	Negative	
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	

3.3. Who should be screened for Hepatitis B infection

The general population should be screened for HBsAg but a priority should be given to the following high risk groups:

- Pregnant women
- Individuals infected with HIV or HCV
- Health care workers exposed to biological fluids
- People who ever received blood or blood products

- Blood or organ donors
- Inmates of correctional facilities
- Household and sexual contacts of HBs Ag-positive person
- Sex workers
- Male having sex with men
- History of unhygienic medical practice or non-medical risk associated activities
- Persons who have ever injected drugs
- Children born to HBV positive mothers
- History multiple sexual partners or STIs
- People with persistently elevated ALT/AST
- Patients undergoing renal dialysis
- Individuals with persistently elevated transaminases

Those at risk and not immune should be offered hepatitis B vaccination.

3.4. Hepatitis B Screening Schedule

Group	Initial	Results	Intervention
High risk groups	Systematic screening every 6 months if not vaccinated	HBsAg-	Provide Vaccine and check HBs Ab
		HBsAg+	Refer to care and treatment
Pregnant woman	Systematic screening at first contact then at delivery if not vaccinated	HBsAg-	Provide Vaccine and check HBs Ab
		HBsAg+	Refer to care and treatment
General population	Propose screening once a year if not vaccinated	HBsAg-	Provide Vaccine and check HBs Ab
		HBsAg+	Refer to care and treatment
Symptomatic	Systematic screening at first contact if not vaccinated	HBsAg-	Provide Vaccine and check HBs Ab
		HBsAg+	Refer to care and treatment

Chapter IV: Management of People with HBV Infection

4.1. Evaluation of patients with chronic HBV infection

4.1.1. The Initial Evaluation

This baseline evaluation includes:

- History and physical examination
- Family history of liver disease, hepatocellular carcinoma (HCC)
- Lifestyle assessment with focus on alcohol consumption and diet
- Laboratory tests to assess liver fibrosis (AST, ALT, Platelets)
- Tests to rule out viral co-infections (Anti-HCV, Anti-HIV)
- Tests to screen for HCC
 - Alpha fetoprotein (AFP) in high risk patients
 - Ultrasound at baseline if available

4.1.2. 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.¹¹

For the purpose of early initiation of patients on therapy, the cutoff of 1.0 should be considered. Below is the formula to be used for APRI Score:

APRI Score and Liver Fibrosis Assessment Formula

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

NB: In this formula, 3 zeros in platelets count are chopped off.

Example, if you have 137,000 platelets, you only consider 137

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

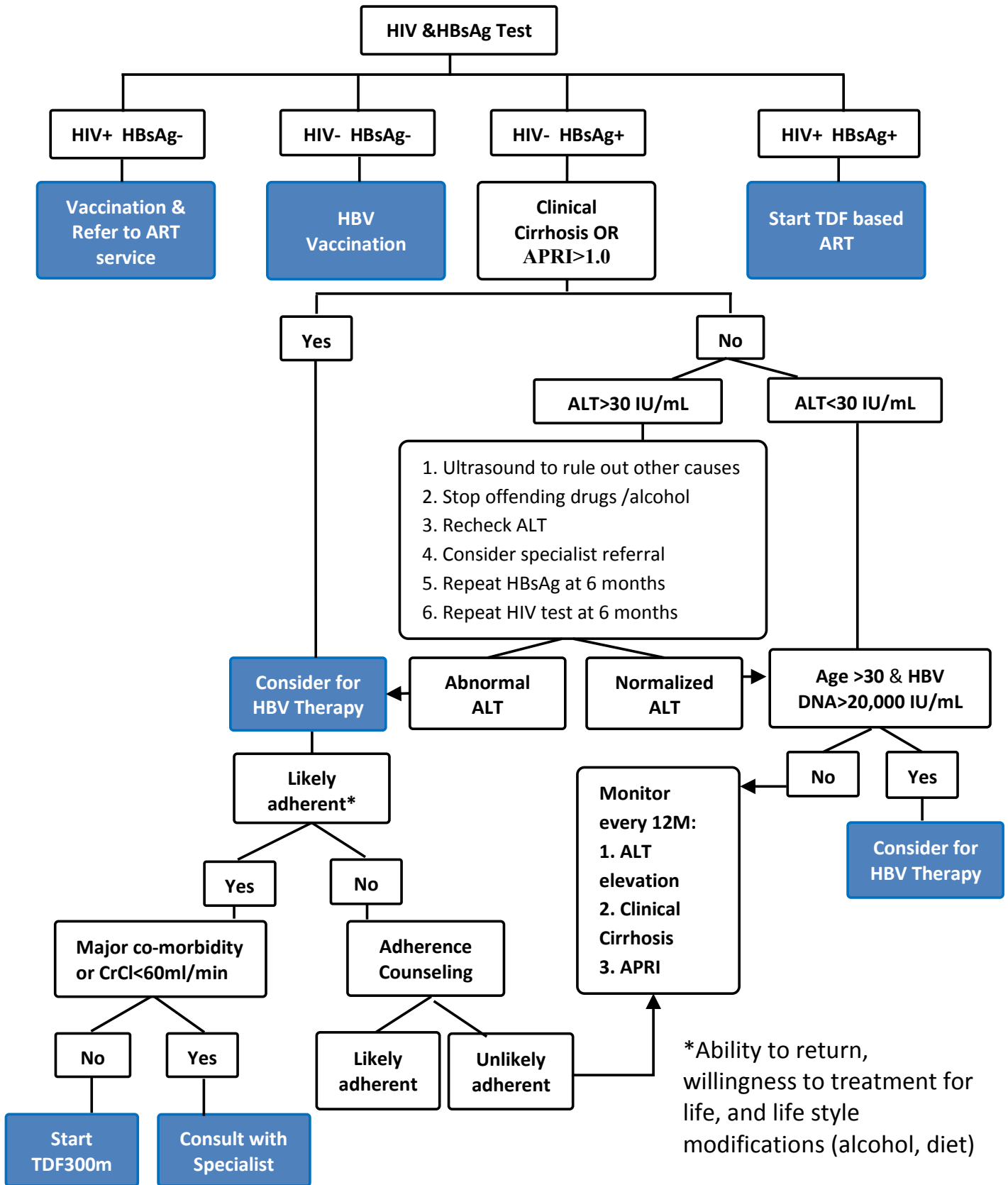
Table 3: Interpretation of Aminotransferase Platelet Ratio Index (APRI)

APRI Value	Interpretation	Action
>1	High Probability (94%) of F4 Cirrhosis	Prioritize for treatment
<1	Risk of Advanced Fibrosis	Consider for treatment

4.1.3. Assessment of HBV Treatment Eligibility

- As a priority, all patients with chronic hepatitis B (CHB) and clinical evidence of compensated or decompensated cirrhosis (or cirrhosis based on APRI score in adults) should be treated, regardless of HBeAg status, ALT or HBV DNA levels¹
- All HIV-HBV co-infected people are eligible to TDF-based regimen for life
- Treatment is also recommended for adults with CHB who do not have clinical evidence of cirrhosis (or based on APRI scores), but are aged more than 30 years, and have persistently abnormal ALT levels or and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL)¹ as shown by figure 2

Figure 2: Diagnosis of HBV and Treatment Eligibility Criteria



4.1.4. Pre-treatment evaluation

This includes:

- Tests to rule out viral co-infections
 - Anti-HCV
 - Anti-HIV
- Tests to screen for HCC
 - Alpha fetoprotein (AFP) in high risk patients,
 - Ultrasound at baseline if available
- Renal Function Test
 - Creatinine
 - Creatinine Clearance (or GFR)
- Education for lifestyle and diet
- Counseling for adherence

4.1.5. Calculation of Creatinine Clearance

The Cockcroft Formula is used to calculate the glomerular filtration rate (GFR) or Creatinine Clearance expressed in mL/min as follows:

If Creatinine machine reports in mg/dL		
(140-Age)x Weight (Kg)		
CrCl=	—————	x 0.85 if woman
72x Creatinine (mg/dL)		
Normal Creat=0.5-1.4		

If Creatinine machine reports in $\mu\text{mol/L}$		
$(140 - \text{Age}) \times \text{Weight (Kg)}$		
CrCl=	0.8172x Creatinine ($\mu\text{mol/L}$)	x 0.85 if woman
Normal Creat=60-120		

Interpretation of Renal Creatinine Clearance	
Value	Interpretation
≥ 90 ml/min	Normal
60-89 mL/min	Mild Renal Insufficiency
30-59 ml/min	Moderate Renal Insufficiency
≤ 29 mL/min	Severe Renal Insufficiency

4.2. Education and Preparation for HBV Treatment

4.2.1. Introduction

In many people with chronic HBV infection, decades can pass between the time of infection and when they develop fibrosis and cirrhosis. During that time, there are health conditions and behaviours that can accelerate the progression of liver damage, including alcohol consumption, substances abuse, diet, obesity, etc.¹²

Furthermore, most clinicians do not often consider life style of patients with acute or chronic hepatitis B while monitoring them before and during therapy yet, this is very critical to the success of patient management.

Patients with chronic hepatitis and liver damage require special diets that need to be worked out for the individual patient so that further liver damage and long-term malnutrition can be prevented.¹³

Therefore, whenever possible, any patient with HBV should be seen by a Clinical Dietician or other trained Counselor for:

- Assessment of alcohol consumption by Alcohol Use Disorders Identification Test (AUDIT) and alcohol reduction interventions
- Smoking and substance involvement screening test (ASSIST)
- Counseling about indications for treatment and adherence to treatment
- Discuss the need for and willingness to commit to long-term treatment, and follow-up monitoring both on and off therapy
- Discuss the importance of full adherence for treatment to be both effective and reduce the risk of drug resistance (and that abrupt cessation of treatment may precipitate acute liver failure)
- Discuss cost implications
- Education on benefits and side-effects
- Advice on lifestyle, appropriate diet and physical activity
- Consider other measures to reduce disease progression in persons with chronic hepatitis B

4.2.2. General Dietary Guidelines for Patients with HBV Infection

Food and drinks pass through the liver to be processed into stored energy and chemicals necessary for life. Then the liver makes nutrients available so the body can use them to build cells, produce energy, and maintain normal body functions.

A bad diet can lead to liver problems. A diet rich in many calories and fats may lead to overweight or obesity linked to the buildup of fat in the liver, called "fatty liver." A fatty liver associated to existing HBV infection will more likely increase risks of developing liver cirrhosis.

A good diet, by contrast, can actually improve liver health in a person with HBV infection. A balanced diet can lead to better liver functioning and lowered risk of cirrhosis of the liver. It also can help the immune system stay strong and fight off illness.

The following dietary guidelines are recommended for people with chronic viral hepatitis:

- Consume more cruciferous vegetables (contains many vitamins, minerals, phytochemicals that assist the body in its detoxification processes)
- Consume more fruits (contains a variety of vitamins, minerals, and phytochemicals that help the liver detoxify)
- Avoid or limit consumption of foods that contain substances that block detoxification (capsaicin, onions, etc.)
- Eat enough protein (to strengthen the body's immune and detoxification systems)
- Limit fat intake, and eat the right fats (a high-fat diet might increase the risk of cirrhosis in patients with chronic hepatitis B)
- Reduce trans fats (hydrogenated oils) and omega-6 fats (safflower oil, sunflower oil, corn oil) and emphasize monounsaturated fats (olive oil, peanut oil) and omega-3 fats
- Increase fiber by increasing consumption of fruits, vegetables, and whole grains helps remove toxins from the gut, relieving some of the burden on the liver)
- Avoid alcohol
- Consume more high-quality, organic foods, as minimally processed as possible
- Avoid non-essential drugs and supplements

- Reduce your exposure to toxins in the environment (such as pesticides) and your workplace (such as chemicals and fumes)

Note: Even natural products have the potential to harm the liver. Consult with your doctor before beginning treatment with any new herb or supplement.

4.3. HBV Treatment Options in Rwanda

4.3.1. Treatment for HBV Mono-infection

Table 4: Treatment for HBV Mono-infection

Option	Drug	Dose	Duration
Preferred	Tenofovir	300mg 1x/day	see endpoint
Alternative*	Entecavir	1mg 1x/day	see endpoint

**Entecavir* is a therapy option for people who cannot take *Tenofovir* or children aged 2-11 years.

4.3.2. Treatment of HIV-HBV Co-infected People

- The diagnosis of HBV infection is based on the presence of HBs Ag and no need to confirm at 6 months
- Those who screen HBs Ag negative should start the HBV vaccine series
- All HIV-HBV infected patients should start treatment for both infections regardless the number of CD4 cells, regardless the WHO clinical staging
- The HIV treatment should include TDF and the treatment is for life

Note:

- a. Patients on second or third line ART should receive additional TDF even if their HIV treatment does not include this.
- b. In case TDF is contraindicated, replace with Entecavir

4.4. HBV Management in Special Patient Groups

4.4.1. Pregnant Women

The treatment criteria for HBV for pregnant women are the same as for the general population. HIV positive pregnant women should receive option B+ containing tenofovir.¹⁴ Tenofovir is the preferred antiviral, because it has a better resistance profile and more extensive safety data in pregnant HBV positive women. For prevention of mother to child HBV transmission, the most important strategy is to deliver the HBV birth dose vaccine as soon as possible after birth, preferably within 24 hours followed by at least two timely subsequent doses and whenever appropriate combined with HBIG within 14 days.

4.4.2. Children

Children usually display an immune tolerant course of their HBV infection. Treatment decision should be taken in consultation with specialist. Entecavir is preferred in younger (2-11 years) children if available. Tenofovir can only be given to children aged ≥ 2 years upon specialist advice.

4.4.3. Healthcare Workers

Healthcare workers need special consideration for HBV screening and HBV vaccination. Those who are HBsAg positive and undertake exposure prone procedures, such as surgeons, gynecologists, nurses, phlebotomists, personal care attendants and dentists, should be considered for antiviral therapy to reduce direct transmission to their patients.

They should receive a potent antiviral agent with a high barrier to resistance (i.e. Tenofovir or Entecavir) to reduce levels of HBV DNA ideally to undetectable or at least to $<2,000$ IU/mL, before resuming exposure-prone

procedures. Post-exposure prophylaxis should be considered following needle stick or other occupational exposures.

4.4.4. Chronic HBV infection with persistently normal transaminases

Chronic HBV infection may present with high level of serum HBV DNA, but persistently normal transaminases. These patients usually have milder hepatic inflammation and tend to have a poor serological response to antiviral therapy. It is recommended to consider HBV treatment if they are > 30 years old with HBV DNA > 20,000 IU/mL otherwise, a regular monitoring of ALT, and signs of cirrhosis (clinical signs and APRI) every 12 months is recommended.

4.4.5. Patients with Compensated Cirrhosis

Treatment should be considered in patients with compensated cirrhosis and detectable HBV DNA levels.

Lifelong TDF therapy is required and regular monitoring of HBV DNA levels is essential.

4.4.6. Patients with Decompensated Cirrhosis

All patients with decompensated cirrhosis should be considered for urgent treatment. Lifelong treatment with Tenofovir or Entecavir is indicated even if the HBV DNA level is low or undetectable in order to improve clinical outcomes, and to prevent flares/reactivation.

4.4.7. Patients with Hepatitis B Drug Resistance

HBV DNA monitoring is critical to detect treatment failure.

- Undetectable HBV DNA levels by real-time PCR (level of detection <10-15 IU/ml) need to be achieved to prevent the development of resistance.
- If HBV DNA levels are still positive, but declining at 48 weeks on Tenofovir or Entecavir, monotherapy can be continued.

- In case of previous treatment with other nucleosides and inadequate treatment response, it is recommended to change to Tenofovir.

4.4.8. HBV and Immunosuppressive Therapy or Cancer Chemotherapy

Approximately 20-50% of HBV carriers undergoing immunosuppressive therapy or cancer chemotherapy develop reactivation of HBV replication, presenting with hepatitis flare and rarely hepatic decompensation. This may occur even in those with occult HBV infection. Administration of Tenofovir prior to these treatments is associated with reduced frequency and severity of hepatitis B flare and improved survival in these patients.

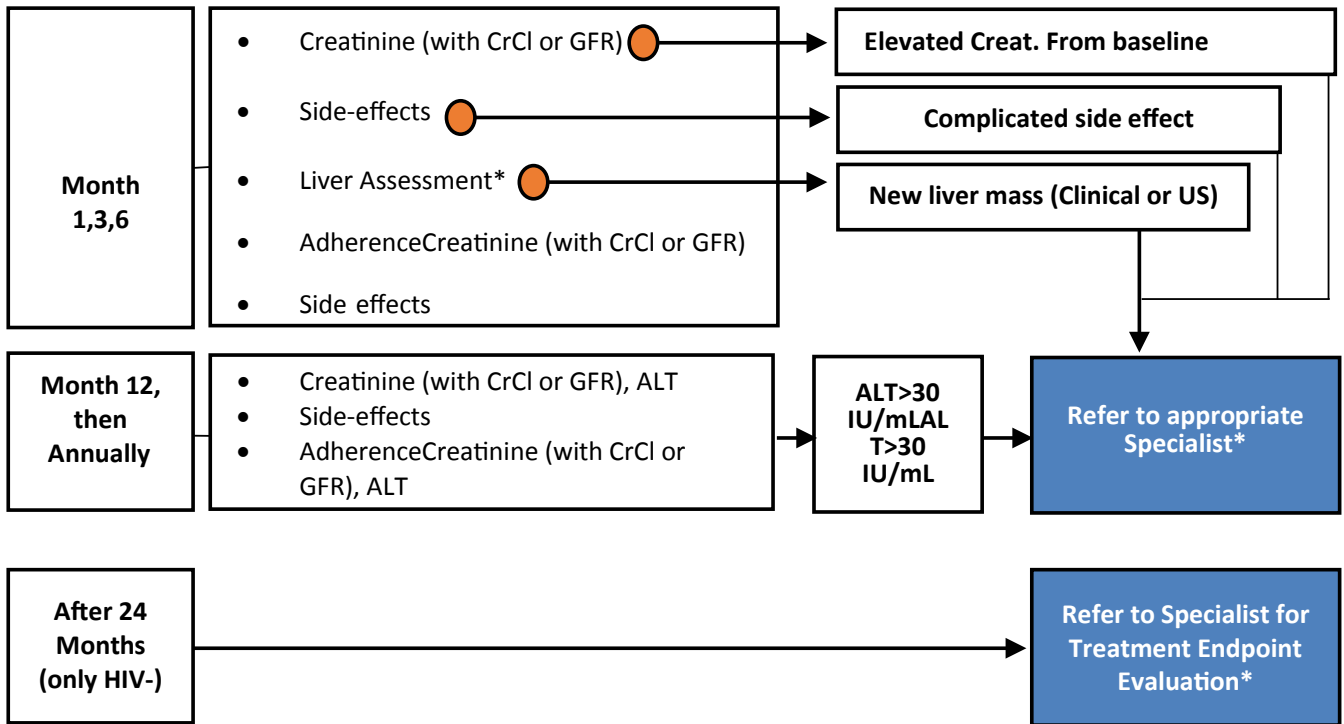
4.5. Follow up of Patients on HBV Treatment

The aim of monitoring during and after treatment is to evaluate the effectiveness of treatment response, treatment adherence, adverse effects of treatment, progression of liver disease and development of HCC, the potential for treatment discontinuation (endpoint), and to identify reactivation early on after treatment discontinuation.

This follow up should involve a multidisciplinary team to achieve the goal of the treatment.

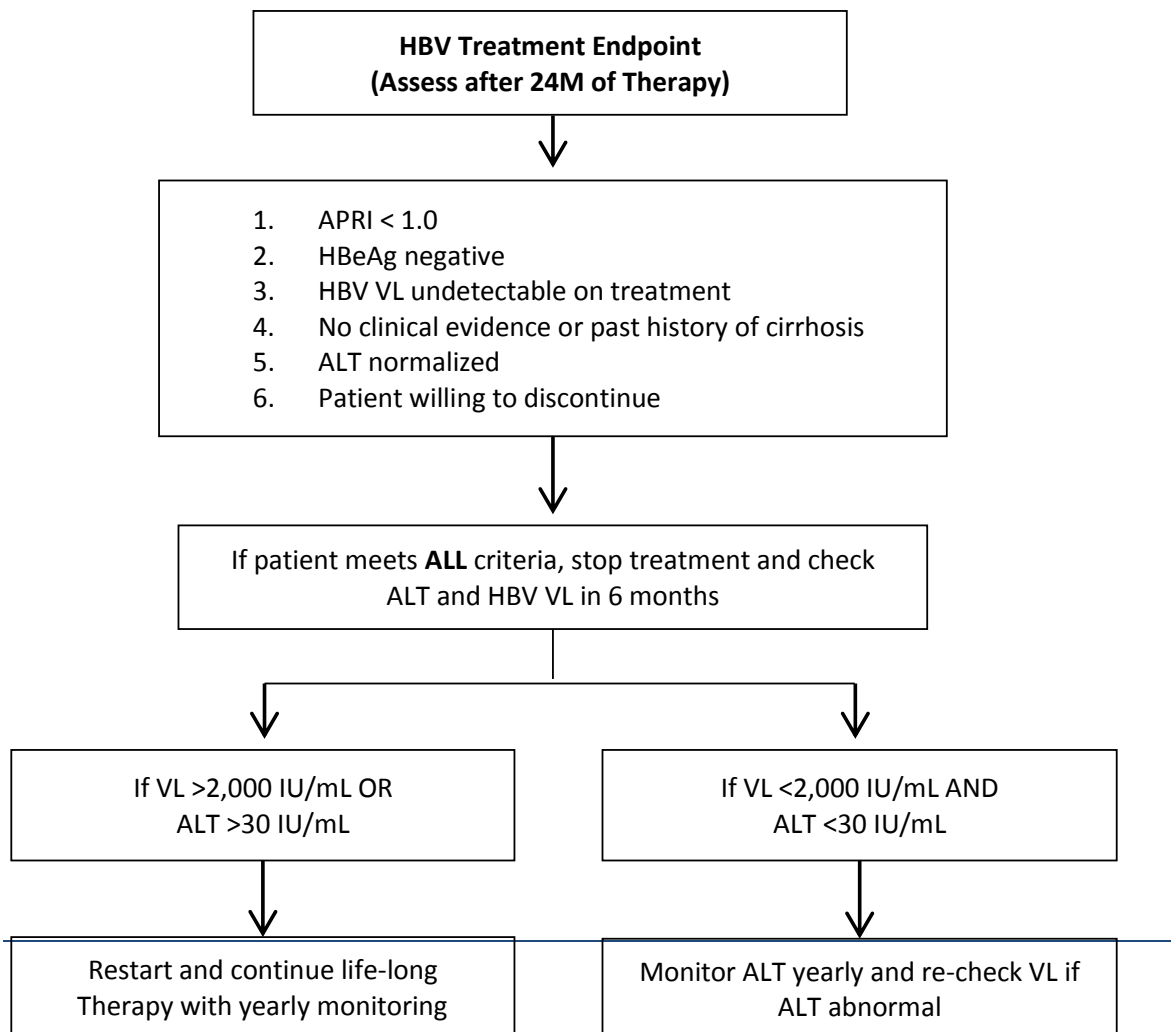
Figures 3 and 4 present the patient's follow up and evaluation for treatment discontinuation (endpoint).

Figure 3: On-Treatment Patient's Follow Up



*NOTE: Patient should be seen by a specialist or a well-trained General Practitioner for treatment discontinuation

Figure 3: HBV Treatment Endpoint Evaluation



PART II:

HEPATITIS C MANAGEMENT

Chapter I: Overview on Hepatitis C

1.1. Definitions

Hepatitis C infection: Inflammation of liver caused by the hepatitis C virus (HCV). HCV is a small, positive-stranded RNA-enveloped virus that is approximately 9.6 kb in length. HCV causes both acute and chronic infection.

Acute HCV: Presence of HCV within six months of acquiring infection.

Chronic HCV: Continued presence of HCV six months or more after acquiring infection.

Sustained virological response (SVR): Undetectable HCV RNA three or six months after the end of treatment.

Non-response: Detectable HCV RNA throughout treatment.

Rapid virological response (RVR): Undetectable HCV RNA 4 weeks after the start of treatment.

Relapse: Undetectable HCV RNA at the end of treatment but detectable HCV RNA within 24 weeks of completing treatment.

Viral breakthrough: Undetectable HCV RNA during treatment followed by detectable HCV RNA during treatment.

1.2. HCV Transmission

HCV is mostly transmitted through exposure to infectious blood. This may happen through transfusions of HCV-infected blood and blood products, contaminated injections during medical procedures, and sharing of needles and syringes among injecting drug users. Sexual or interfamilial transmission is also possible, but is much less common.⁸

1.3. Groups at high risk of Hepatitis C

- People who have received medical or dental interventions in healthcare settings where infection control practices are inadequate
- Patients who received blood products or organ transplants prior to the introduction of anti-HCV screening (HCV screening started in Rwanda in 1999)
- People who inject drugs (PWID)
- People who have had tattoos, body piercing, scarification or traditional surgical procedures done where infection control practices are substandard
- Children born to mothers infected with HCV
- People with HIV infection
- People who have used intranasal drugs
- Prisoners and previously incarcerated people
- Men having sex with men
- Female sex workers

Chapter II: Prevention of Viral Hepatitis C Infection

In the absence of a vaccine for hepatitis C, prevention of HCV infection depends upon reducing the risk of exposure to the virus. This is challenging because of the various routes of transmission and the different populations that are affected.³ Prevention activities aim at reducing or eliminating potential risk for HCV transmission.

As for HBV infection, most people who are infected with HCV are unaware of their chronic infection. They are at high risk of developing severe chronic liver disease and can unknowingly transmit the infection to other people.

The prevention of hepatitis C infection consists of primary, secondary and tertiary prevention.

2.3. Primary Prevention of Hepatitis C Infection

The primary prevention of hepatitis C infection consists of activities aimed at reducing or eliminating potential risk for HCV transmission such as increasing awareness and knowledge of the general and high risk population in HCV transmission and prevention.

The following are specific areas of HCV primary prevention:

2.3.1. Communication for Behavior Change

- Increased awareness and knowledge of HCV transmission and prevention and control of the general population
- Provide specific message to increase awareness and knowledge of HCV transmission and prevention and control in the high risk groups
- Training of health care providers

2.3.2. Infection Control Precautions in Community Settings

- Harm reduction practices for injecting drug users prevent HCV transmission.
- Avoid unsafe practices around non-medical or traditional practice (cosmetic, scarification, tattoos, circumcision procedures, traditional medical practice among others)
- Safe household practice (handling or sharing of sharp objects, sharing toothbrushes, hand washing, safe blood contact, avoid intimate contact with carriers among others)
- Safe injections for IVDU
- Promotion of correct and consistent condom use
- Avoid multiple partners, seek regular screening and treatment for STIs
- Routine screening of sex workers
- Integrated action to eliminate discrimination and gender violence, and to increase access to medical and social services for vulnerable people

2.3.3. Prevention of HCV Infection in Health-care Settings

Occupational safety measures to prevent transmission of viral hepatitis to health care workers through:

- Hand hygiene including surgical hand preparation, hand washing and use of gloves
- Safe handling and disposal of sharps and waste
- Safe cleaning of equipment
- Testing of donated blood and blood products
- Improved access to safe blood and blood products
- Training of health personnel
- Follow standard universal precautions with open cuts or bleeding

- Safe injections in medical facilities
- Screening of the general population for HCV
- Management of HCV infected patients including health care providers

2.3.4. Recommendations for HCV Post Exposure Prophylaxis

A. Immediate Care of the Exposed Person

After exposure to blood or other body substances, the following is recommended as soon as possible:

- Wash the wound site with soap and water
- If eyes are contaminated then rinse them, while they are open, gently but thoroughly with water or normal saline
- If blood or other body substances get in the mouth, spit them out and then rinse the mouth with water several times
- If clothing is contaminated remove clothing and shower with soap
- Where water is not available use of a non-water cleanser or antiseptic should replace the use of soap and water for washing cuts or punctures of the skin or intact skin

B. Specific Measures for prevention of Hepatitis C

At present there is no prophylaxis proven to be effective following exposure to HCV. The aim of follow up is to detect hepatitis C so that appropriate management can be instituted.

- The person should be informed and advised on the risk of transmission to secondary contacts, especially during the first 6 months following the incident
- The exposed person should have baseline testing for HCV antibody, if negative be retested at 6 months for HCV as well as for other blood borne viruses

- If HCV antibody is positive, the person should be referred for HCV PCR testing and follow up if necessary

2.4. Secondary and Tertiary Prevention of HCV Infection

This prevention aims at early detection of HCV infection for timely treatment and follow up before any advanced liver disease but also reduces HCV transmission.

The early diagnosis helps infected people to take precautions to protect the liver from additional harm by abstaining from alcohol and tobacco consumption, avoiding certain toxic drugs and adopting appropriate diet.

It is therefore advised to screen asymptomatic individuals with focus on high risk groups to provide appropriate counseling and close follow up to those who screen HCVAb positive.

Chapter III: Screening and Diagnosis of HCV Infection

3.1. Screening and Diagnosis of HCV Infection

Screening for HCV infection is done using HCV serological testing. If positive, a NAT for HCV RNA assay is needed to confirm chronic HCV infection. Several screening assays have been evaluated by WHO, and sensitivity, specificity, and positive and negative predictive value results are available.¹⁵ HCV diagnosis depends on the presence of HCVAbs. Anti-HCV are generally not detectable in patients with initial signs or symptoms of hepatitis C.¹⁶ Anti-HCV develop in acute infection generally between 2 and 8 weeks after evidence of liver injury. Some people may not test positive for 6-9 months after onset of illness.¹⁷ Hepatitis C viremia may be detected by RT-PCR within days after infection.¹⁸

In general, screening for hepatitis C should be done with anti-HCV by ELISA-based test, and positive samples should be confirmed by PCR.¹⁶

- In Rwanda, the screening of HCV will be done based on the presence of HCVAbs (ELISA or Rapid Test) then confirmed with PCR
- If PCR is positive, the patient will be confirmed HCV-positive and evaluated for treatment initiation.
- If PCR is negative, the patient will be informed that the infection has been cleared and will receive appropriate counseling for prevention (Figure 5).

3.2. Who should be screened?

Anybody seeking HCV screening should be offered the service. However, the high risk groups for HCV are recommended for systematic screening.

3.3. Hepatitis C Screening Schedule

Group	Initial	Results	Intervention
High risk groups	Systematic screening every 12 months	HCVAb-	Educate for behavior change
		HCVAb+	Refer to PCR-RNA
Pregnant woman	Systematic screening at first contact	HCVAb-	Educate for behavior change
		HCVAb+	Refer to PCR-RNA
General population	Propose screening every 12 months	HCVAb-	Educate for behavior change
		HCVAb+	Refer to PCR-RNA
Symptomatic	Systematic screening at first contact	HCVAb-	Educate for behavior change
		HCVAb+	Refer to PCR-RNA

Chapter IV: Treatment of HCV Infection

4.1. Initial Evaluation of HCV-infected Patients

HCV-infected patients should be evaluated for the presence or development of chronic liver disease (CLD), and treatment eligibility¹⁹.

Hepatic transaminases reflect liver inflammation but their values fluctuate and may be normal with advanced liver disease. CT scan or ultrasound is the preferred method for the detection of hepatocellular carcinoma.

To evaluate liver fibrosis, liver biopsy is considered as the gold standard method. There are other noninvasive methods to stage the liver disease, but they are variable in sensitivity and specificity²⁰.

In Rwanda, as a resource-limited setting country, we recommend that the aminotransferase/platelet ratio index (APRI) be used for the assessment of hepatic fibrosis and where possible, other noninvasive tests that require more resources such as elastography (Fibroscan) can be used.

Liver function is assessed by clinical examination, and the following laboratory analysis:

- ALAT/ASAT
- Hematology (hemoglobin, platelets and leucocytes including differential count)
- Alpha-fetoprotein (AFP) if warranted
- Ultrasound if available

Patients for whom treatment is not being pursued should have their APRI checked every 12 months.

APRI Score and Liver Fibrosis Assessment Formula

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

NB: In this formula, 3 zeros in platelets count are chopped off.
Example, if you have 137,000 platelets, you only consider 137

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

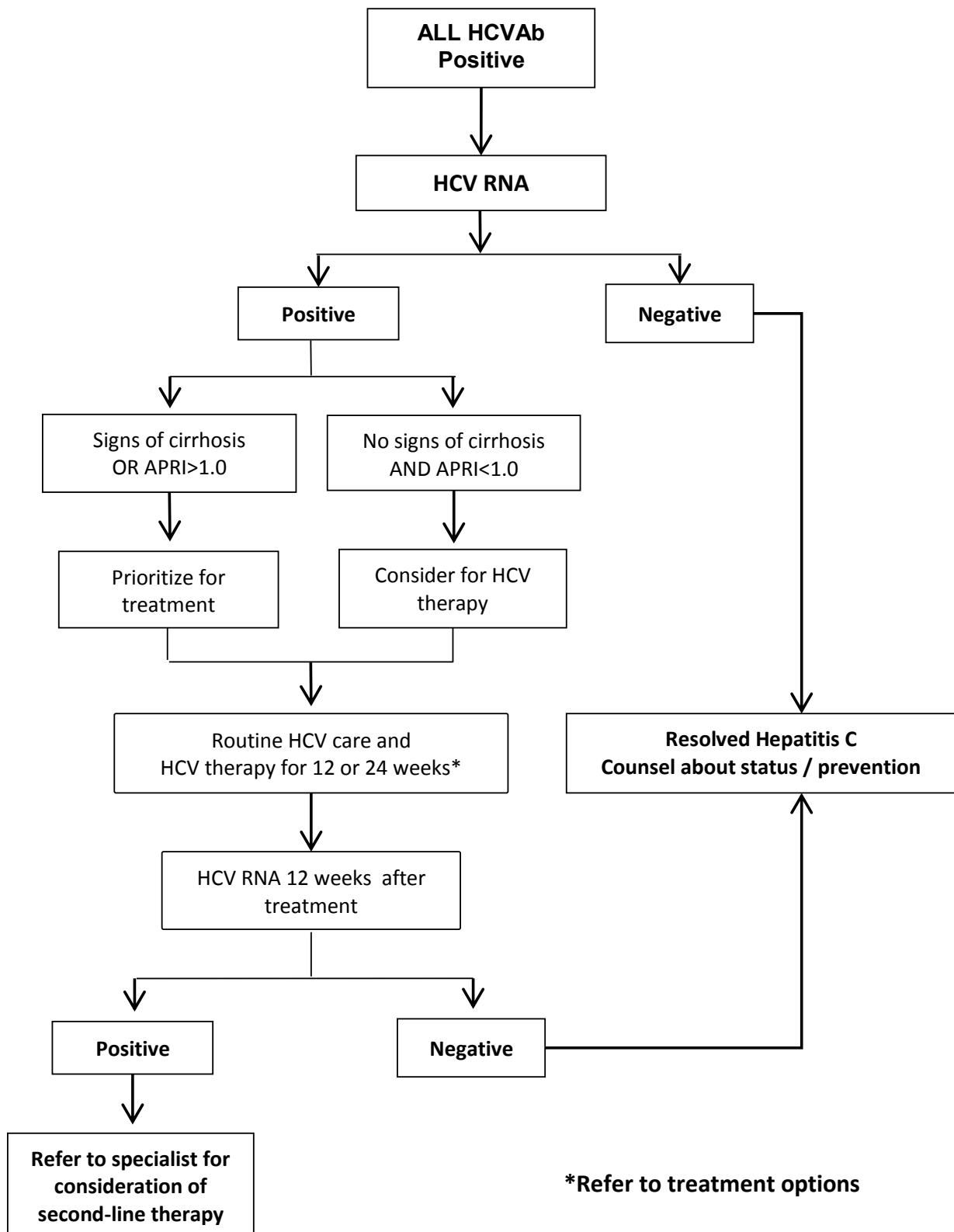
Interpretation of Aminotransferase Platelet Ratio Index (APRI)

APRI Value	Interpretation	Action
>1	High Probability (94%) of F4 Cirrhosis	Prioritize for treatment
<1	Risk of Advanced Fibrosis	Consider for treatment

A strategy that uses a combination of the high and low cut-off values was assessed. Using this strategy, patients with values above the APRI high cut-off value would be prioritized for treatment as they have a high probability (94%) of having cirrhosis.¹

A pretreatment liver biopsy is not mandatory but may be helpful in patients with normal transaminase levels, particularly those with a history of alcohol dependence, in whom little correlation may exist between liver enzyme levels and histology findings.²¹

Figure 4: HCV Diagnosis and Treatment Algorithm



4.2. Treatment of HCV Mono-infection

4.2.1. HCV Treatment Indications

The goal of the treatment is to eradicate the virus, prevent liver cirrhosis and its complications including hepatocellular carcinoma (HCC).²²

All patients with chronic hepatitis C infection should be considered potential candidates for drug therapy.²³

Treatment is strongly recommended for patients who are at risk of developing cirrhosis, generally defined by a measurable hepatitis C RNA level and APRI >1.0 or liver biopsy showing portal or bridging fibrosis along with moderate inflammation and necrosis.

Patients with advanced fibrosis and cirrhosis (METAVIR stages F3 and F4 or APRI >1.0) should be prioritized for treatment as they are at higher risk of developing cirrhosis and hepatocellular carcinoma¹. Persons with less advanced fibrosis (APRI <1.0) could also be considered for treatment (Figure 5).

4.2.2. Education and Preparation for HCV Treatment

As for HBV infection, it can take decades for HCV infected people to develop fibrosis and cirrhosis. During that time, there are health conditions and behaviours that can accelerate the progression of liver damage, including alcohol consumption, substances abuse, diet, obesity, etc.

Furthermore, most clinicians do not often consider life style of patients with acute or chronic hepatitis C while monitoring them before and during therapy yet, this is very critical to the success of patient management.

Patients with chronic hepatitis and liver damage require special diets that need to be worked out for the individual patient so that further liver damage and long-term malnutrition can be prevented.

Therefore, whenever possible, any patient with HCV should be seen by a clinical dietician or a trained counselor for:

- Assessment of alcohol consumption and alcohol reduction interventions
- Smoking and substance involvement screening test
- Counseling about indications for treatment and adherence to treatment
- Discuss the importance of full adherence for treatment to be both effective and reduce the risk of drug resistance
- Discuss cost implications
- Education on benefits and side-effects,
- Advice on lifestyle, appropriate diet* and physical activity
- Consider other measures to reduce disease progression in persons with chronic hepatitis C

***General dietary and lifestyle recommendations for HCV infected people are the same as for patients with HBV infection**

4.2.3. HCV Treatment Options

Table 5:HCV Treatment Options in Rwanda

Option	Drug 1	Drug 2	Duration	Notes
1	Sofosbuvir 400mg OD	Ribavirin (1,000-1,200 mg) Weight-based Dose)	24 weeks	Ribavirin contra-indicated in pregnant women and their partners, needs monitoring of Hemoglobin
2	Sofosbuvir 400mg	Ledipasvir 90mg	12 weeks	Fixed-dose combination
3	Sofosbuvir 400mg OD	Daclatasvir 60mg*	12 weeks	*DCV 90mg daily for co-administration with Efavirenz and 30mg daily with Ritonavir

Notes

- Ribavirin and/or Pegylated Interferon can be added to any of these regimens for re-treatment of treatment failures.
- Avoid interferon products in cirrhotic patients
- If using Ribavirin, haemoglobin (Hb) needs to be done before starting therapy and then at 2 and 4 weeks after starting:
 - Start Ribavirin only if Hb>10g/dL
 - Hb<10g/dL reduce Ribavirin by 200mg each week until Hb ≥ 10g/dL
 - If Hb ≤ 8g/dL then stop Ribavirin for 2 weeks then resume at 600mg daily (or 200mg lower than last administered dose) and monitor Hb weekly
 - While Hb <10g/dL monitor Hb weekly
- Renal failure and Ribavirin:
 - CrCl 30-50 mL/min use 200mg alternating with 400mg daily
 - CrCl <30 mL/min or haemodialysis use 200mg daily

4.3. Management of HIV/HCV Co-infection

4.3.1. Introduction

According to the WHO guidelines for the management of Hepatitis C, published in 2014, co-infection with HIV adversely affects the course of HCV infection, and co-infected people have a significantly accelerated progression of liver disease to cirrhosis, decompensated liver cirrhosis and HCC compared to HCV mono-infected people, particularly those with advanced immunodeficiency (CD4 count <200 cells/mm³).¹

Furthermore, co-infected patients have a lower likelihood of achieving sustained virological response to treatment compared with mono-infected ones. Two large European cohorts have shown that after ART initiation, CD4 recovery was impaired in HIV/HCV-coinfected persons when compared to those infected with HIV alone. HIV/HCV co-infected patients also demonstrated more rapid HIV disease progression compared to those who were HIV mono-infected, and had an impaired recovery of CD4 cells.¹

4.3.2. National Recommendations for HIV/HCV co-infection

- Whenever possible, HIV-infected patients should be screened for HCV infection, preferably before starting ART.
- Treat all regardless of CD4 cell count.
- Initial ART combination regimens for most HIV/HCV co-infected patients are the same as those for individuals without HCV infection.
- However, when treatment for both HIV and HCV is indicated, consideration of potential drug-drug interactions and overlapping toxicities should guide ART regimen selection or modification.

- Although ART should be initiated for most HIV/HCV co-infected patients regardless of CD4 cell count, in ART naive patients with CD4 counts >500 cells/mm³, it is recommended to defer ART until completion of HCV treatment.
- In patients with <200 CD4 cells/mm³, it is recommended to initiate ART and delay HCV therapy until patient is clinically able to tolerate the treatment.

4.3.3. ART and anti-HCV Combinations

People with HIV require special consideration regarding the selection of an antiretroviral regimen. The safety profile in HCV/HIV-1 co-infected subjects treated with Sofosbuvir is similar to that observed in HCV-mono-infected subjects. Elevated total bilirubin (grade 3 or 4) occurs extremely commonly in persons treated with Sofosbuvir and Atazanavir as part of the antiretroviral regimen. Tipranivir/Sofosbuvir is not recommended. Darunavir/ritonavir, Efavirenz, Emtricitabine, Raltegravir, Rilpivirine and Tenofovir have been tested and no dose adjustment is currently recommended.

✓ Sofosbuvir

Sofosbuvir is considered to have relatively few clinically significant drug-drug interactions, but coadministration of sofosbuvir with the following medications is not recommended because these medications may significantly lower sofosbuvir levels:

- Anticonvulsants: carbamazepine, oxycarbazepine, phenobarbital, and phenytoin
- Antimycobacterials: rifabutin, rifampin, rifapentine
- Herbal Supplements: St. John's wort

- HIV Protease Inhibitors: tipranavir-ritonavir
- The concentration of Sofosbuvir decreases in presence of tipranavir/ritonavir and co-administration is not recommended.
- No clinically significant interactions of Sofosbuvir with Darunavir/ritonavir, Efavirenz, Emtricitabine, Raltegravir, Rilpivirine, or Tenofovir

✓ **Ledipasvir:**

Ledipasvir undergoes minimal metabolism and expectations are that this medication will have few clinically significant drug-drug interactions.

✓ **Daclatasvir:**

Daclatasvir is a HCV NS5A replication complex inhibitor. It can interact with Efavirenz and Atazanavir/Ritonavir.

It is therefore recommended to adjust DCV dose at 90mg daily for co-administration with Efavirenz and 30mg daily with Ritonavir.

✓ **Pegylated IFN and Ribavirin**

Do not combine pegylated interferon-alpha and ribavirin treatment with:

- **Didanosine** (increased to toxic levels and may lead to mitochondrial toxicity and lactate acidosis)
- **Zidovudine** (may worsen the anemia caused by ribavirin)

Summary HCV-HIV Drugs Interactions				
HIV Drug	Sofosbuvir	Ledipasvir	Daclatasvir	Ribavirin
TDF				
ABC				
AZT				Anemia++
3TC				
DDI				Lactic Acidosis, Mitochondrial Toxicity
FTC				
EFV			DCV ↘	
ETV				
NVP				
Rilpivirine				
Darunavir/r				
Tipranavir/r	SOF ↘			
Lop/r				
ATV/r			DCV ↗	Monitor Bilirubinemia
RAL				
Rifampicin	SOF ↘			
Rifabutin	SOF ↘			
Not Recommended				
Recommended				
Recommended with attention				
No Study Found				

4.4. Management of Patients with HCV and Cirrhosis

Between 15% and 30% of persons infected with HCV will go on to develop cirrhosis of the liver within 20 years and a proportion of these will progress to HCC.²⁴

Persons with compensated cirrhosis have the least time available for treatment, the most to lose and much to gain from achieving SVR. HCV treatment must be commenced before the onset of decompensated disease and IFN-containing regimens must be avoided unless there is no other option.³

In addition to clinical care offered to all HCV patients with blood tests for ALAT, cirrhotic patients should be reviewed by a doctor for liver failure care.

Ribavirin is predominantly excreted by kidneys and the drug should normally not be used in patients with a creatinine clearance <60mL/min²⁵. On an individual basis ribavirin maybe administered cautiously to patients with renal failure. This requires careful monitoring of hemoglobin and plasma ribavirin levels and this treatment should be centralized at referral centers.

4.5. HCV Infected Patient Monitoring

4.5.1. General recommendations

No laboratory monitoring is required except when using ribavirin or interferon. Patients can be seen at intervals of 4 weeks for adherence and side-effect assessment during treatment and need a HCV RNA at the end of treatment to assess for treatment response.²⁶

Ribavirin and interferon use requires more intensive monitoring for side-effects (see HCV treatment algorithms).

4.5.2. Common Side Effect of Hepatitis C Antiviral Agents

Table 6: Common Side Effect of Hepatitis C Antiviral Agents

Molecule	Side Effects
Interferon	<ul style="list-style-type: none"> - Fever, Fatigue - Muscle/joint pain - Nausea, Diarrhea, Drymucosa - Psychic instability, Depression, Aggravation of preexisting epilepsy - Bone marrow depression - Visual disturbance - Hyper-and hypothyroidism dermatitis, Alopecia
Ribavirin	Anemia and may cause dyspepsia and rash. Birth defects have been produced in animal experiments and contraception should be used during treatment and until 4 month after (female)/7 month after (males) end of treatment
Sofosbuvir	Fatigue and Headache
Ledipasvir	Fatigue, headache, insomnia, and nausea
Daclatasvir	Nausea; headache; fatigue; anemia; lymphocytopenia; neutropenia.

PART III:

VIRAL HEPATITIS PROGRAM IMPLEMENTATION

1. Introduction

Successful implementation of the recommendations in these guidelines and establishment of affordable screening, treatment and care programs in the public and private sectors for people with chronic hepatitis B and C infections in Rwanda will depend on a well-planned process of adaptation and integration into national strategies and guidelines. The implementation of the recommendations in these guidelines should be informed by local context, including national health systems, laboratory capacity, supply systems for drugs and other commodities, availability of financial resources, the organization and capacity of the health system and anticipated cost-effectiveness of the various interventions. Given differences in health facilities capacity (personnel and laboratory), the viral hepatitis program will be implemented by establishing a minimum package of services at each level of implementation.

In general, viral hepatitis services include a prevention message, screening, diagnosis of both HBV and HCV for those in need in accordance to available capacities, initiation of treatment and patients follow up including specific counseling and timely referral of complicated cases to higher level according to the national guidelines.

The central level will ensure the coordination of the guidelines implementation at all levels through medical procurement, training and clinical mentorship for healthcare providers, supervision and monitoring and evaluation of programs at national level.

2. Minimum Package of Services

Viral Hepatitis B and C related services have to be integrated in the already existing health care delivery systems.

For a better coordination, the following minimum package of services to be offered to the population was defined based on the available resources and capacity of each level of health facility.

Minimum Package for Viral Hepatitis B&C Services per Level of Health Facility			
Level/Provider	Prevention	Laboratory	Treatment
Community - HCWs	<ul style="list-style-type: none"> - Prevention message - Provide information to the community 	<ul style="list-style-type: none"> - Provide information to the community 	<ul style="list-style-type: none"> - Program adherence support - Provide information to the community
Health Center - Nurse - Counsellor - Laboratory Technician	<ul style="list-style-type: none"> - Prevention message - Vaccination of new born - Adults vaccination - Post exposure prophylaxis - Capacity building of CHWs 	<ul style="list-style-type: none"> - Rapid tests for screening - Liver function tests - Renal function tests - Hematology 	<ul style="list-style-type: none"> - Clinical assessment for cirrhosis - Assess eligibility criteria for HBV and HCV using available capacities - Counselling (adherence, lifestyle) - Initiate HBV treatment for simple cases - Follow up of patients on HBV and HCV treatment - Refer complicated cases to the next level as appropriate
District Hospital - General Practitioner - Nurse - Laboratory Technician - Counsellor - Nutritionist	<ul style="list-style-type: none"> - Prevention message - Vaccination of new born - Adults vaccination - Post exposure prophylaxis - Supervision and clinical mentorship of Health Centers 	<ul style="list-style-type: none"> - Rapid tests for screening - Liver function tests - Renal function tests - Hematology - Capacity building of Lab Technicians at Health Center Level (Training, Mentorship) 	<ul style="list-style-type: none"> - Clinical assessment for cirrhosis - Counselling (adherence, lifestyle) - Assess eligibility criteria for HBV and HCV using available capacities - Initiate HBV treatment for intermediary complicated cases - Follow up of patients on HBV and HCV treatment - Refer complicated cases to the next level as appropriate - Capacity building of Nurses at Health Center Level (Training, Mentorship)
Referral Hospital - Specialist, - General Practitioner - Nurse - Laboratory Technician - Counsellor - Nutritionist	<ul style="list-style-type: none"> - Prevention message - Vaccination of new born - Adults vaccination - Post exposure prophylaxis - Capacity building of medical at District Hospitals (Training, Mentorship, Supervision) 	<ul style="list-style-type: none"> - Rapid tests for screening - Liver function tests - Renal function tests - Hematology - ELISA Tests - Viral Load Monitoring - Capacity building of medical at District Hospitals (Training, Mentorship, Supervision) 	<ul style="list-style-type: none"> - Counselling (adherence, lifestyle) - Advanced clinical assessment for cirrhosis - Assess eligibility criteria for HBV and HCV using available capacities - Initiate HBV treatment complicated cases - Initiate HCV treatment - Follow up of patients on HBV and HCV treatment - Provide guidance on HCV and HBV end of treatment - Capacity building of medical at District Hospitals (Training, Mentorship, Supervision)

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