NATIONAL GUIDELINES FOR PREVENTION AND MANAGEMENT OF VIRAL HEPATITIS B, C AND SEXUALLY TRANSMITTED INFECTIONS

May 2019
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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.

The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus.

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

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Dr Diane GASHUMBA
Minister of Health
PREFACE

Viral Hepatitis B&C is characterized by the inflammation of liver cells, and may cause hepatocellular carcinoma (HCC) and cirrhosis if not treated. HBV and HCV infection can be either acute or chronic, and the associated illness ranges in severity from asymptomatic to symptomatic, progressive disease. Chronic hepatitis B (CHB) and chronic hepatitis C (CHC) are major public health problems. According to recent WHO statistics, worldwide, there are an estimated 257 million HBV chronically infected persons, 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. For Viral Hepatitis C, more than 71 million people around the world have chronic HCV infection.

The majority of people are unaware of their HBV and their HCV infection. For the lucky ones who have been diagnosed, treatment remains inaccessible and with the current HIV pandemic, the viral hepatitis and HIV co-infection remains critical.

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. However, although current HBV treatment can’t cure the disease, universal hepatitis B immunization programs that target infants, with the first dose at birth, have been highly effective in reducing the incidence and prevalence of hepatitis B in many endemic countries.

Hepatitis C infection differs from other chronic viral infections such as HIV and HBV as it can now be cured using antiviral active treatments. Several medicines are available to treat persons infected with HCV, and cure rates have steadily improved with the introduction of newer medicines since 2012. These new medications can cure more than 90% of persons with HCV infection and are effective against genotypes that were previously difficult to treat.

Around the world, more than a million Sexually Transmitted Infections (STIs) are acquired every day. STIs can have serious consequences such as increasing the risk of HIV acquisition, cervical cancer and pelvic inflammatory disease and in cases of mother-to-child transmission, increase risk of adverse birth outcomes. Syndromic management of STIs, relying on clinical algorithms that allow health workers to diagnose infections based on observed syndromes, is often recommended in low resource settings.
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<th>Full Form</th>
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<tr>
<td>AFP</td>
<td>Alpha Feto-Protein</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immuno Deficiency Syndrome</td>
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<tr>
<td>ALT</td>
<td>Alanine aminotransferase</td>
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<tr>
<td>Anti-HBe</td>
<td>Antibody to Hepatitis B e antigen</td>
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<td>Anti-HBs</td>
<td>Antibody to the Hepatitis B surface antigen</td>
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<tr>
<td>Anti-HCV</td>
<td>Antibody to the Hepatitis C Virus</td>
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<td>APRI</td>
<td>Aminotransferase to Platelet Ratio Index</td>
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<td>ART</td>
<td>Antiretroviral Therapy</td>
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<tr>
<td>AST</td>
<td>Aspartate aminotransferase</td>
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<tr>
<td>CBC</td>
<td>Complete Blood Count</td>
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<tr>
<td>cccDNA</td>
<td>Covalently closed circular DNA</td>
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<td>CD4</td>
<td>Cluster of Differentiation 4</td>
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<tr>
<td>CHB</td>
<td>Chronic Hepatitis B</td>
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<tr>
<td>CHC</td>
<td>Chronic Hepatitis C</td>
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<td>CHW</td>
<td>Community Health Workers</td>
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<tr>
<td>CKD</td>
<td>Chronic Kidney Disease</td>
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<td>CLD</td>
<td>Chronic Liver Disease</td>
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<tr>
<td>CrCl</td>
<td>Creatinine Clearance</td>
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<tr>
<td>DAA</td>
<td>Direct Acting Antiviral</td>
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<tr>
<td>DCV</td>
<td>Daclatasvir</td>
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<tr>
<td>DDI</td>
<td>Drug-Drug Interaction</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>eGFR</td>
<td>Glomerular Filtration Rate</td>
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<tr>
<td>ELISA</td>
<td>Enzyme-Linked Immuno Sorbent Assay</td>
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<tr>
<td>GFR</td>
<td>Glomerular Filtration Rate</td>
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<tr>
<td>GP</td>
<td>General Practitioner</td>
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<tr>
<td>Hb</td>
<td>Hemoglobin</td>
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<tr>
<td>HBeAg</td>
<td>Hepatitis B Virus Early Antigen</td>
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<tr>
<td>HB1g</td>
<td>Hepatitis B Immunoglobulin</td>
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<tr>
<td>HBsAg</td>
<td>Hepatitis B surface Antigen</td>
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<td>HBV</td>
<td>Hepatitis B Virus</td>
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<td>HCC</td>
<td>Hepatocellular Carcinoma</td>
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<td>HCV</td>
<td>Hepatitis C Virus</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>IFN</td>
<td>Interferon</td>
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We acknowledge that guidelines are living documents and as such, they need to evolve along with changes in the scientific landscape. We therefore encourage all interested parties (healthcare providers, patients, policy makers, etc.) to share their feedback with the working group to enable us to improve the quality of the guidelines in the future.

We believe that the guidelines will be instrumental in strengthening the management of hepatitis B, hepatitis C and STIs, which in turn will improve the health and well-being of the Rwandan population.
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PART I: HEPATITIS B INFECTION MANAGEMENT
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Dr Diane GASHUMBA
Minister of Health
Chapter I: Generalities on Hepatitis B Infection

1.1 Definitions

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

**Acute HBV Infection:** Presence of HBs Ag 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 HBVDNA concentrations. May result in seroconversion from HBeAg to anti-HBe (antibody to hepatitis B e antigen).

**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.

**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.

**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.

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

**Treatment interruption:** Missing one drug collection appointment at treating health facility (eg. Missing a monthly appointment of dose collection).

**Lost to follow-up:** The patient is said to be lost to follow-up when he/she missed appointment of treating health facility during 3 months.

**Persistently normal/abnormal ALT:** Three (3) ALT determinations below or above the upper limit of normal, made at unspecified intervals during 6-12month period or predefined intervals during a 12month period.
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-familiar, child-to-child.
- Shared syringe use (for health facilities or intravenous drug users)
- Other unhygienic medical practice (razors, inadequate sterilization, dental and surgical procedures)
- Unhygienic practice of non-medical risk associated activities, such as manicures, tattoos, toothbrush sharing, traditional surgical and scarification practice, hair salons etc.

1.3 Groups at High Risk of Hepatitis B Infection
- People who ever received unsafe blood or blood products (before 1985)
- Individuals infected with HIV or HCV
- Inmates of correctional facilities
- Persons who have ever injected drugs
- Health care workers exposed to biological fluids
- Pregnant women
- Children born to HBV positive mothers
- Household and sexual contacts of HBs Ag-positive person
- Patients undergoing renal dialysis
- Persons needing immunosuppressive therapy
- Sex workers
- Men having sex with men (MSM)
- History of multiple sexual partners or STIs

Chapter 1 Summary: Generalities on Hepatitis B Infection
Chapter 1 details definitions related to viral hepatitis B infection, its disease course, immunological markers, transmission routes and high-risk groups. During the disease course, progression of disease may not be linear and patients may progress from immune-tolerant to immune-active, immune-inactive or reverse.
- **Acute HBV Infection:** Presence of hepatitis B surface antigen (HBsAg) with or without clinical symptoms lasting less than 6 months
- **Chronic HBV Infection:** Persistence of hepatitis B surface antigen (HBs Ag) for 6 months or more after acute infection with HBV
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. 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 on HBV transmission and prevention among general and high-risk population. The following are specific areas of HBV primary prevention:

2.1.1. Communication for Behaviour Change
- Increase awareness, knowledge and behavior change on HBV transmission, prevention among the general population and high-risk groups;
- Train health care providers on HBV transmission, prevention and behavior change

2.1.2. Infection Control Precautions in Community Settings
- Avoid unsafe practices: cosmetic, scarification, tattoos, circumcision practice and tooth extraction out of medical settings, etc.
- Harm reduction practices for injecting drug users to prevent HBV transmission.
- Safe household practice (avoid handling or sharing sharp objects, sharing toothbrushes, blood contact, unprotected sexual contact with carriers etc.)
- Safe injections for Intravenous Drug User (IVDU)
- Promote 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
- Vaccinate HBs Ag negative sexual partners of persons with hepatitis B infection.
- Put in place integrated actions to eliminate discrimination and gender violence and increase access to medical and social services to victims of gender violence

2.1.3. Prevention of HBV infection in health-care settings

Put in place occupational safety measures to prevent transmission of viral hepatitis to health care workers through:
o Hand hygiene including surgical hand preparation, hand washing and use of gloves
o Safe handling and disposal of sharps and waste
o Safe cleaning of equipment
o Testing of donated blood and blood products
o Improved access to safe blood and blood products
o Training of health care personnel
o Follow standard universal precautions with open cuts or bleeding
o Safe injections in medical facilities
o Management of HBV infected patients including health care providers

2.1.4. HBV vaccination

2.1.4.1. HBV birth dose vaccine
The HBV birth dose vaccine consists of a single dose monovalent vaccination administered within 24 hours of birth to all babies. HBV birth dose should be followed by (two or) three routine doses of HBV vaccine as per the current Hepatitis B vaccination schedule administered at Week 6, 10 and 14 of life. Subsequent routine doses of HBV vaccine are co-administered with diphtheria, tetanus, whooping cough and haemophilus influenza type B as part of the pentavalent vaccine\(^3\).

2.1.4.2. Routine adult vaccination for HBV
Hepatitis B vaccine is recommended for all children aged 0-18 years. It is recommended for infants beginning at birth in the hospital; all older children who did not get all the recommended doses of hepatitis B vaccine as an infant should complete their vaccine series as soon as possible; adolescents who were not vaccinated as well as adults at increased risk of acquiring HBV infection. In addition, the vaccine can be given to any person who desires protection from hepatitis B.

Blood testing before vaccination is recommended for children and adults born in countries where HBV is endemic. HBsAg negative people receive HBV vaccine for their protection and HBsAg positive people don’t need the vaccine, they are referred to care and treatment. (See algorithm in Figure 2). Vaccinating a person already immune to or infected with HBV will not help or harm the person (See Table 1 for vaccine schedule).

In case of interruption of vaccine schedule, vaccine series should be continued rather than restarted. When possible, HBV antibody titer can be measured at least 2 months after last dose of vaccine to assess the level of the immune response. Present and past household and sexual contacts of individuals positive for HBsAg are recommended to receive HBV vaccination if they screen negative for HBsAg or to be linked to care if positive.
Table 1: Hepatitis B vaccination schedule in Rwanda

<table>
<thead>
<tr>
<th>Nº</th>
<th>Group</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Newborn</td>
<td>&lt; 24 Hours</td>
<td>Week 6</td>
<td>Week 10</td>
<td>Week 14</td>
</tr>
<tr>
<td>2</td>
<td>HIV+ Adult</td>
<td>M0</td>
<td>M1</td>
<td>M6</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>HIV- Adult</td>
<td>M0</td>
<td>M1</td>
<td>M2</td>
<td>M6</td>
</tr>
</tbody>
</table>

Note:
- It is recommended to vaccinate babies within 24 hours after birth to prevent mother to child transmission but also to prevent HBV infection before their 6th week of life when they start pentavalent vaccines.
- The dosage for adult is 1ml and 0.5ml for newborns.
- The dose is doubled (2 ml) in HIV-positive adult people.
- Counseling for screening of HBsAg prior to vaccination.
- When vaccine schedule is interrupted, vaccine series should be continued rather than restarted.

2.1.5. HBV Post-Exposure Prophylaxis

2.1.5.1. 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, gently but thoroughly rinse eyes while open with water or normal saline;
- If blood or other body substances are consumed in mouth, spit substances and rinse mouth with water several times;
- If clothing is contaminated remove clothing and shower with soap;
- When water is unavailable, wash cuts or skin punctures with non-water cleanser or antiseptic

2.1.5.2. Specific Measures

Hepatitis B exposure management depends on the following:

- The HBV immuno-status of the exposed person
- Level of protection of exposed individual (fully or partially immunized and/or immune)

Exposed individuals with no immunity to HBV should ideally be administered first dose of HBV vaccine within 24 hours of exposure as an active immunization. Passive immunization against hepatitis B with Hepatitis B Immunoglobulin (HB Ig) given within 24 hours and up to 14 days of exposure is also recommended. In case HB Ig is not available, the active immunization (HBV vaccine alone) is recommended (Fig. 1).
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**

The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus.

These guidelines would not have been finalized without the usual 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 hepatitis technical working group and respective organizations that contributed to the development of this document.

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2.1.6. Prevention of Mother to Child Transmission (PMTCT) of HBV

All pregnant women should be screened for HBsAg during pregnancy and all babies should receive HBV birth dose vaccine within 24 hours after birth to prevent mother to child transmission but also to prevent HBV infection before they are enrolled in national child immunization program with pentavalent vaccines at their 6th week of life. Given the fact that HBV is mainly transmissible to babies during delivery, HBV vaccine within 24 hours after birth, combined with HB Ig (when available) should be administered to infants born to mothers who are HBsAg positive.

In HBV infected pregnant women, eligibility criteria and indications for treatment are the same as for other adults, and treatment with Tenofovir is recommended.
All HBsAg positive pregnant women who are eligible for HBV treatment based on the algorithm should start long term HBV treatment during pregnancy to prevent the HBV transmission to their babies. When a pregnant woman was on entecavir or any other regimen before pregnancy, it is recommended to switch to tenofovir based regimen. For HBV/HIV coinfected adults, adolescents and children aged 3 years and older, tenofovir + lamivudine (or emtricitabine) + efavirenz as a fixed-dose combination is recommended as the preferred option to initiate ART \(^3\)\(^{10}\).

### 2.2. Secondary and Tertiary Prevention of Hepatitis B 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.

<table>
<thead>
<tr>
<th>Preventing Mother to Child Transmission of HBV: Summary Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Screen all pregnant women for HBV during pregnancy</td>
</tr>
<tr>
<td>• Follow up positive mothers and start HBV treatment during pregnancy if eligible</td>
</tr>
<tr>
<td>• Vaccinate all babies within 24 hours after birth to prevent mother to child transmission but also to prevent HBV early childhood infection before their 6(^{th}) week of life when they start pentavalent vaccines.</td>
</tr>
</tbody>
</table>

The early diagnosis helps infected people to take precautions to protect the liver form additional harm by abstaining from alcohol and tobacco consumption, avoiding certain toxic drugs and adopting appropriate diet\(^8\). 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 2 Summary: Hepatitis B Prevention

Hepatitis B infection consists of primary, secondary and tertiary prevention. Primary prevention consists of all measures put in place before the onset of the disease while secondary and tertiary preventions aim at preventing complications of the disease after its onset. The most critical primary prevention measure is vaccination against HBV. Table1 details recommended vaccination schedule in Rwanda. Hepatitis B can be transmitted from HBV-infected pregnant mother to her child during pregnancy or perinatal period.

The most important strategy to prevent mother-to-child transmission of HBV is the administration of the **birth dose vaccine** to the child within 24 hours after birth but also the **administration of HBV treatment to pregnant mothers confirmed HBV positive and eligible to treatment**. To avoid infection, all potential sources of contact with infected individuals should be avoided.
Lastly, secondary and tertiary prevention measures are also necessary for early detection and treatment but also reduction of transmission and prevention of disease complications.

Chapter III: Screening and Diagnosis of Hepatitis B Infection

3.1 Diagnosis of Hepatitis B Infection
3.1.1 Early Detection for Prevention of Advanced Liver Disease

Viral hepatitis B is a silent epidemic. Most acute HBV infections are asymptomatic or cause mild symptoms, which are often unrecognized\(^3\). Acute infection may cause nonspecific symptoms and clinical signs, such as:

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

Around 5-10% of adults acutely infected with hepatitis B virus progress to chronic infection and stay in preclinical phase for decades\(^4\). Early diagnosis helps infected people 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 HBs Ag positive.

The recommended diagnosis of hepatitis B virus infection is the evaluation of the patient’s blood for hepatitis B surface antigen (HBsAg).

- The presence of HBsAg confirms infection (acute or chronic)
- 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 individuals is indicative of chronicity.
- When available, other markers as detailed in the table below (HBsAg, Anti-HBs, Anti-HBc, and IgM Anti-HBc) can help confirm chronicity of infection.
3.2 Interpretation of HBV serologic markers

<table>
<thead>
<tr>
<th>Tests</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Negative</td>
<td>Susceptible to infection</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Negative</td>
<td>Immune due to natural infection</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>Negative</td>
<td>Immune due to Hepatitis B vaccination</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>Positive</td>
<td>Acutely infected</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Negative</td>
<td>Chronically infected</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

3.3 Who should be screened for Hepatitis B infection

General population should be screened for HBsAg with priority for the following high risk groups. Those at risk and not immune should be offered HBV vaccination.

- Individuals infected with HIV or HCV
- Health care workers exposed to biological fluids
- People who received blood or blood products before 1990
- Pregnant women
- Children born to HBV-infected mothers
- Blood or organ donors
- Inmates of correctional facilities
- Household and sexual contacts of HBs Ag-positive person
- History of unhygienic medical practice or non-medical risk associated activities
- Persons who have ever injected drugs
- Sex workers
- Men having sex with men
- History of multiple sexual partners or STIs
- Patients undergoing renal dialysis
- Individuals with persistently elevated transaminases
3.4 Diagnosis of hepatitis B

The diagnosis of hepatitis B should be done by assessing the presence of HBsAg using ELISA test or Rapid Diagnostic Tests (RDTs) (Figure 2). In HIV-infected populations and for cirrhotic patients, a single positive HBsAg test is indicative of chronicity and the patient should be initiated on treatment for HBV as applicable (Refer to section 4.2.).

The WHO recommended a single HBsAg test to all countries where HBsAg prevalence is >0.4% basing on the rationale that most of people are infected during childhood and already suffer from chronic HBV. When HBsAg is positive, further treatment eligibility follows (See Figure 3).

*The presence of a single positive HBsAg in patients with clinical cirrhosis and/or APRI score > 2 and/or in PLHIV indicates chronicity and is a criterion for a direct initiation of HBV treatment. (See Figure 3)
3.5 Hepatitis B screening schedules

Table 2: Hepatitis B screening schedules

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

Chapter 3 Summary: Screening and Diagnosis of Hepatitis B Infection

Early detection of HBV infection helps prevent advanced liver disease. It is thus recommended that everyone should be screened for Hepatitis B Infection although priority is given to high-risk populations such as pregnant women, healthcare providers, HIV-infected populations, sex workers, prisoners and children born to HBV-infected mothers.

Screening for hepatitis B infection is done through assessing presence of HBsAg using ELISA test or rapid diagnostic tests (RDTs). In the general population, the presence of a single positive HBsAg using Elisa or RDT test calls for further evaluation of treatment eligibility. In HIV-infected populations, cirrhotic persons and patients with APRI score > 2, the presence of a single positive HBsAg is indicative of chronicity and calls for direct HBV treatment.
Chapter IV: The Management of People with Hepatitis B 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, over the counter, traditional medicine and diet
- Laboratory tests to assess liver fibrosis (AST, ALT, Platelets) and HBV DNA if possible
- Tests to rule out viral co-infections: Anti-HCV and Anti-HIV
- Tests to screen for HCC
  - Alpha fetoprotein (AFP) in high risk patients,
  - Ultrasound at baseline

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. 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**

$$APRI = \frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}} \times \frac{\text{Platelet Count (10}^9/\text{L})}{2}$$

<table>
<thead>
<tr>
<th>APRI Value</th>
<th>Interpretation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2</td>
<td>High probability of fibrosis and/or cirrhosis</td>
<td>Prioritize for treatment</td>
</tr>
<tr>
<td>≤2</td>
<td>Potential risk of advanced Fibrosis</td>
<td>Consider for treatment if persistently high transaminases without any other explanations (ex. Drug or alcohol-abuse etc.)</td>
</tr>
</tbody>
</table>

---

1 An online calculator can be found at: [http://www.hepatitisc.uw.edu/page/clinical-calculators/apri](http://www.hepatitisc.uw.edu/page/clinical-calculators/apri)
4.1.3 Assessment of HBV Treatment Eligibility

*When HBV DNA test is unavailable, 3 ALT determinations during a period of 6-12 months may guide treatment. 3 successive abnormal ALT suggest the initiation of HBV treatment after ruling out other causes of abnormal ALT.

**The presence of a single positive HBsAg in patients with clinical cirrhosis or APRI score > 2 or in PLHIV indicates chronicity and calls for a direct HBV treatment. HBV DNA test is only done for the purpose of monitoring, first as a baseline test before treatment but also for continuous monitoring while on treatment.
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 levels.

All HIV-HBV co-infected people are directly eligible to TDF/TAF-based regimen for life included in their HIV regimen.

Treatment is also recommended for all infants and adults (especially people aged above 30 years) with CHB who do not have clinical evidence of cirrhosis (or based on APRI scores) and/or evidence of high-level HBV replication (HBV DNA >20 000 IU/mL) (Figure 3).

4.1.4 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:

\[
\text{CrCl} = \frac{(140-\text{Age}) \times \text{Weight (Kg)}}{72 \times \text{Creatinine (mg/dL)}} \times 0.85 \text{ if woman}
\]

Normal Blood Creatinine = 0.5-1.4

\[
\text{CrCl} = \frac{(140-\text{Age}) \times \text{Weight (Kg)}}{0.8172 \times \text{Creatinine (µmol/L)}} \times 0.85 \text{ if woman}
\]

Normal Blood Creatinine = 60-120

<table>
<thead>
<tr>
<th>Interpretation of Renal Creatinine Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
</tr>
<tr>
<td>≥ 90 mL/min</td>
</tr>
<tr>
<td>60-89 mL/min</td>
</tr>
<tr>
<td>30-59 mL/min</td>
</tr>
<tr>
<td>≤ 29 mL/min</td>
</tr>
</tbody>
</table>
4.2 Education and Preparation for HBV Treatment

4.2.1 Introduction

Decades can pass between the time of HBV infection and when patients develop fibrosis and cirrhosis. During that time, there are health conditions and behaviors that can accelerate the progression of liver damage, including alcohol consumption, substances abuse, obesity, etc. Clinicians often do not consider patient life style while monitoring patient therapy. Yet lifestyle is very critical to the success of patient management. Therefore, whenever possible, any patient with HBV should receive clinical guidance on the following topics: Alcohol consumption and alcohol reduction interventions.

- Smoking and substance involving screening test
- Counselling about indications for treatment and adherence to treatment including risk of acute liver failure upon abrupt cessation of treatment and risk of drug resistance in case of poor adherence
- Discussion on the willingness to commit to lifelong treatment, its cost implications, and follow-up monitoring both on and off therapy
- Education on benefits and side-effects,
- Advice on lifestyle and physical activity

4.2.2 General Dietary Guidelines for Patients with HBV Infection

Patients with chronic hepatitis B should avoid consumption of alcohol since it accelerates the process of liver fibrosis and cirrhosis, should strive for a balanced diet including proteins, lipids, carbohydrates, fruits and vegetables.

4.3 HBV Treatment Options in Rwanda

4.3.1 Treatment for HBV Mono-infection \textsuperscript{10, 11}

Table 4: Treatment options for Hepatitis B infection in Rwanda

<table>
<thead>
<tr>
<th>Age/ category</th>
<th>Drug</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\geq 12) years</td>
<td>Tenofovir (TDF or TAF)</td>
<td>Adult: 300mg 1x/day Children (\geq 12) years, if recommended by a physician</td>
<td>Lifelong treatment recommended (Exceptionally, see treatment endpoint)</td>
</tr>
<tr>
<td>\textsuperscript{2} 2 - 11 years or people with intolerance to Tenofovir</td>
<td>Entecavir</td>
<td>Adult: 1mg 1x/day Children: Dependent on weight and age</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{2} Entecavir is a therapy option for adults who cannot take Tenofovir such as people with renal failure and preferred therapy for children aged 2-11 years based on weight and age
Chronic HBV is generally asymptomatic in children under 2 years of age who are generally immune-tolerant. A conservative approach to treatment is generally indicated and in exceptional cases of cirrhosis or necro-inflammatory disease, refer to a specialist for treatment.

4.3.2 Treatment of HIV-HBV Co-Infected People
The diagnosis of HBV infection is based on the presence of HBs Ag which confirms the chronicity if the person is already HIV positive. Those who screen HBs Ag negative should directly start HBV vaccine series. All HIV-HBV infected patients should start treatment for both infections as per new HIV “treat all” guidelines. HIV treatment should include TDF/TAF and the recommended treatment is for life.

Note:
- HIV-HBV co-infected patients on HIV second or third line ART should receive additional TDF/TAF even if their HIV treatment does not include this.
- In case Tenofovir is contraindicated, replace it with Entecavir if accessible.

4.4 HBV Treatment in Special Patient Groups
4.4.1 HBV Infection and Pregnancy
The treatment criteria for HBV in pregnancy are the same as in the adult population. HIV positive pregnant women should receive ART regimen containing TDF/TAF\textsuperscript{12}. TDF/TAF is the preferred antiviral, because it has a better resistance profile and more extensive safety data in pregnant HBV-positive women. Breastfeeding is not contraindicated in HBs Ag untreated women or on TDF based regimen or prophylaxis, except when the mother has cracked, damaged, or bleeding nipples, or in the context of HIV coinfection\textsuperscript{18}.

4.4.2 Hepatitis B in 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 children aged 2-11 years in Rwanda. It should be taken under strict supervision of specialist and dosage will differ based on weight and age of the child.\textsuperscript{3}

\textsuperscript{3} Entecavir doses in treatment-naive children older than 2 and at least 10 kg are: 0.15 mg (10-11 kg), 0.2 mg (>11-14 kg), 0.25 mg (>14-17 kg), 0.3 mg (>17-20 kg), 0.35 mg (>20-23 kg), 0.4 mg (>23-26 kg), 0.45 mg (>26-30 kg), and 0.5 mg (>30 kg). For treatment-experienced children older than 2 and at least 10 kg,
4.4.3 Hepatitis B in Healthcare Workers
Health-care 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 persons. 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, preferably before resuming exposure-prone procedures.

4.4.4 Chronic HBV infection with persistently normal transaminases
Chronic HBV infection may be present with high level of serum HBV DNA, but persistently normal transaminases. These patients usually have mild hepatic inflammation and tend to have a poor serological response to antiviral therapy. It is recommended to prioritize them for HBV treatment if 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 Treatment of Patients with Compensated Cirrhosis
Treatment should be prioritized in patients with compensated cirrhosis and detectable HBV DNA levels. The diagnosis of HBV infection is based on the presence of HBs Ag and there is no need to wait for other tests if the person is already cirrhotic. Cirrhosis can be diagnosed with characteristic findings on ultrasound (nodularity, splenomegaly) or with APRI>2.0. Life-long TDF/TAF therapy should be directly started after a single HBs Ag test and regular monitoring of HBV DNA levels is essential.

4.4.6 Treatment of Decompensated Cirrhosis
Management of patients with decompensated cirrhosis who are infected with HBV is complex. Such patients should be referred to a specialist. 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. For this category of patients as well, a single HBs Ag test is enough to initiate treatment.

the entecavir doses are: 0.30 mg (10-11 kg), 0.4 mg (>11-14 kg), 0.5 mg (>14-17 kg), 0.6 mg (>17-20 kg), 0.7 mg (>20-23 kg), 0.8 mg (>23-26 kg), 0.9 mg (>26-30 kg), and 1.0 mg (>30 kg)
4.4.7 Treatment of Drug-Resistant Hepatitis B

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 after 48 weeks of treatment to prevent resistance;
- If HBV DNA levels are still positive, but declining at 48 weeks on Tenofovir or Entecavir, monotherapy can be continued;
- If HBV DNA is still detectable without declining while on treatment, check the causes like poor adherence and reinforce counselling;
- In case of previous treatment with other nucleosides and inadequate treatment response, it is recommended to change to Tenofovir if applicable.

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 recommended and it is associated with reduced frequency and severity of hepatitis B flare and improved survival in these patients.

4.4.9 Treatment in Patients with Renal Failure

TDF should not be given to patients with renal failure. For HBV patients with renal failure, the preferred drug is Entecavir with renal adjustments. Tenofovir Alafenamide Fumurate (TAF) can also be considered in the absence of Entecavir.

4.5 Follow-up of Patients on HBV Treatment

4.5.1 Patient Follow-up on Treatment

The aim of monitoring during (and after treatment if applicable) 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, and early identification of reactivation in cases of treatment discontinuation.

This follow-up should involve a multidisciplinary team to achieve the goal of the treatment.
Figure 4: Patient’s follow-up and evaluation

4.5.2 Treatment adherence

**Non-adherent patients:** Adherence to treatment for this group will be assessed using standard procedures. This means will assess if patients have taken all prescribed drugs. Poor adherent patients encompass the following conditions:

Poor adherence may encompass any of the following:
- Missing more than 5% of prescribed doses during the last three months.
- Missing appointments (at least one clinical / pharmacy visit without any notification).
- Viral load detectable after 48 weeks’ post-initiation of treatment and at two consecutive times (every 12 months)

**Lost to follow-up:** For the application of these guidelines in Rwanda, a patient is considered as lost to follow-up, if this patient missed one pharmacy visit and was not seen for the last 3 months from the last drugs pickups by a peer educator and health care providers were not able to reach him/her by any communication mean (telephone call and home visit) within one month from the time he/she was expected to attend the clinic.

4.5.3. Treatment endpoint

**4.5.3.1. Background**

Although nucleos(t)ide analogues (NAs) are potent inhibitors of HBV DNA replication, they do not result in cure, because NA therapy does not eliminate the replicative template cccDNA in the nucleus or integrated viral genome. Therefore, although there are considerable advantages of finite NA therapy, both for patients and policy-makers, long-term maintenance suppressive therapy is generally required. Exceptionally, a finite duration of treatment may be possible in some HBeAg-positive persons who achieve anti-HBe seroconversion and a sustained undetectable HBV DNA viral load with some other additional criteria as described later in this part of the chapter.
4.5.3.2. Lifelong NA therapy
All persons with cirrhosis based on clinical evidence (or APRI score >2 in adults) as well as HIV-HBV co-infected patients require lifelong treatment with NAs, and should not discontinue antiviral therapy because of the risk of reactivation, which can cause severe acute-on-chronic liver injury.

4.5.3.3. Discontinuation
The main goals of antiviral therapy in patients with chronic HBV are to improve survival and quality of life by preventing progression to severe liver disease (decompensated cirrhosis and liver failure), HCC and death. This can be achieved by suppressing HBV DNA to undetectable levels and a life-long HBV treatment is highly recommended. HBsAg loss and/or seroconversion is considered to be the optimal goal of antiviral therapy, and a marker of sustained treatment response in both HBeAg positive and HBeAg negative persons, but is achieved in only a minority of HBeAg positive persons (10–15% after 5 years), and rarely in those who are HBeAg negative. HBeAg seroconversion in HBeAg positive persons may also be considered as a potential stopping point to guide treatment cessation, but again is infrequent even with potent NAs. Discontinuation of HBV treatment is associated with high risk of reactivation and relapse of the disease and may be considered exceptionally in:

- persons without clinical evidence of cirrhosis (or based on APRI score ≤2 in adults);
- and who can be followed carefully long term for reactivation;
- and if there is evidence of HBeAg loss and seroconversion to anti-HBe (in persons initially HBeAg positive) and after completion of at least one additional year of treatment;
- and in association with persistently normal ALT levels and persistently undetectable HBV DNA levels (where HBV DNA testing is available).
- Where HBV DNA testing is not available: Discontinuation of NA therapy may be considered in persons who have evidence of persistent HBsAg loss and after completion of at least one additional year of treatment, regardless of prior HBeAg status.
HBV treatment Endpoint Evaluation

Figure 5: HBV treatment Endpoint Evaluation

4.5.3.4. Retreatment

Relapse may occur after stopping therapy with NAs. Retreatment is recommended if there are consistent signs of reactivation (HBsAg or HBeAg becomes positive, ALT levels increase, or HBV DNA becomes detectable again) (where HBV DNA testing is available)
Chapter 4 Summary: The Management of People with Hepatitis B Infection

Treatment Eligibility
After chronicity of hepatitis B infection is confirmed, an initial evaluation considers factors such as liver function, age, liver fibrosis, and HBV DNA level. APRI score should be calculated for all patients using formula below:

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

Equation 1.

Patients eligible for treatment:
- Co-infection with HIV (no further evaluation for treatment eligibility needed)
- Cirrhotic (compensated or decompensated)
- Patients with APRI score > 2.0
- High-level HBV DNA replication (> 20,000 UI/mL)

Among those who are not HIV co-infected, not cirrhotic, treatment eligibility is mainly based on high-level HBV DNA replication (> 20,000 UI/mL) and sometimes, when there is no VL capacity, it may be based to persistently abnormal ALT.

Treatment
Patients eligible for treatment should be informed of the lifelong nature of treatment and agree to fully adhere to treatment regimen. Preferred treatment in Rwanda for chronically infected adults is daily dose of TDF/TAF (300mg/day) for life. For infected children and patients with renal impairment, the preferred drug is Entecavir. Patients co-infected with HIV-HBV should start treatment for both infections as per new HIV “treat all” guidelines. HIV treatment should include TDF/TAF and the recommended treatment is for life. Exceptionally, discontinuation of HBV treatment may be considered but it is associated with high risk of reactivation and relapse of the disease.
### Treatment options for Hepatitis B infection in Rwanda (see table 4)

<table>
<thead>
<tr>
<th>Age/ category</th>
<th>Drug</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 12 years</td>
<td>Tenofovir</td>
<td>Adult: 300mg 1x/day</td>
<td>Lifelong treatment recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Children ≥ 12 years, if recommended by a physician</td>
<td></td>
</tr>
<tr>
<td>2 - 11 years</td>
<td>Entecavir</td>
<td>Adult: 1mg 1x/day</td>
<td>(Exceptionally, see endpoint)</td>
</tr>
<tr>
<td>or people with intolerance to Tenofovir</td>
<td></td>
<td>Children: Dependent on weight and age</td>
<td></td>
</tr>
</tbody>
</table>

Special care should be taken when managing and treating the following patient groups as detailed in Part I Section 4.4 of the guidelines: pregnant women, children, healthcare workers, patients with decompensated cirrhosis, patients with drug-resistant HBV, patients with immunosuppression, and patients with renal failure.

**Regular follow-up of patients** initiated on treatment is crucial to ensuring treatment adherence, monitoring potential side effects and monitoring development of HCC among patients with cirrhosis. The following assessment should be done during follow-up: creatinine-levels, ALT, side-effects and adherence.

---

4 Entecavir is a therapy option for adults who cannot take Tenofovir such as people with renal failure and preferred therapy for children aged 2-11 years based on weight and age)
KEY MESSAGE FOR HBV MANAGEMENT

1. HBV is diagnosed by the detection of a single HBs Ag.

2. Acute HBV is characterized by acute presence / absence of clinical symptoms, abnormal liver tests and disappearance of HBs Ag within 6 months.

3. Chronic HBV is recognized by persistence of HBs Ag more than 6 months.

4. Immunization against HBV infection for all non-immune individuals is the best strategy for HBV prevention. Other prevention measures consist of avoiding all risk contacts with potential HBV infection sources.

5. All pregnant women should be systematically screened for HBV. To prevent MTCT, positive pregnant women eligible to treatment should start HBV treatment. In addition, all babies should be vaccinated within 24 hours after birth to prevent MTCT.

6. In HIV infected patients, cirrhotic or patients with APRI score > 2, the presence of a single HBs Ag automatically refers to the chronicity of HBV and treatment.

7. Treatment eligibility criteria in chronic HBV include:
   - HIV-HBV coinfection
   - Cirrhosis
   - APRI score > 2.0;
   - DNA > 20,000 IU / mL;
   - Persistently elevated ALT where DNA test cannot be performed;

8. HBV treatment is rarely indicated in children but can be provided for children aged 2 years and above and, in this case, the drug of choice is Entecavir.

9. HBV treatment for pregnant women is the same as for other adult persons.

10. Treatment monitoring should be done to optimize adherence to treatment, detect signs of treatment success /failure (eg. Liver function tests) and manage treatment related side effects.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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. The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus. These guidelines would not have been finalized without the usual 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 hepatitis technical working group and respective organizations that contributed to the development of this document.

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Dr Diane GASHUMBA
Minister of Health
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Dr Diane GASHUMBA
Minister of Health
Chapter I: Generalities on HCV Infection

1.1 Definitions

**Hepatitis C infection:** Inflammation of liver caused by Hepatitis C Virus (HCV). The hepatitis C virus is a small, positive-stranded RNA-enveloped virus which can cause both acute and chronic infection.

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

**Chronic HCV:** Continued presence of anti-HCV and HCV RNA six months or more after acquiring infection

**Sustained virological response (SVR):** Undetectable HCV RNA 12 weeks 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 12 weeks after completing treatment

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

1.2 HCV Transmission

Hepatitis C virus (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.13

1.3 Groups at high risk of Hepatitis C

- Persons who have received medical or dental interventions in health-care settings where infection control practices are substandard
- Patients who received blood products or organ transplants prior to the introduction of anti-HCV screening (HCV screening started in Rwanda in 1999)
- Persons who inject drugs (PWID)
- Persons 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
- Persons with HIV infection
- Persons who have used intranasal drugs
- Prisoners and previously incarcerated persons
- Men having Sex with Men
- Female Sex Workers
Chapter 1 Summary: Generalities on HCV Infection

Chapter 1 details definitions related to viral hepatitis C infection, its disease course, immunological markers, transmission routes and high-risk groups. 55-85% of patients infected with acute HCV will progress into chronic hepatitis C infection.

- **Acute HCV**: Presence of HCV within six months of acquiring infection
- **Chronic HCV**: Continued presence of anti-HCV and HCV RNA six months or more after acquiring infection.
Chapter II. Prevention of HCV Infection and disease progression

Prevention of HCV infection depends on reducing or eliminating potential risk of exposure to the virus. Most people who are chronically infected with HCV are unaware. They are at high risk of developing severe chronic liver disease and can unknowingly transmit the infection to other people.

2.1 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 among the general and high-risk population.

The following are specific areas of HCV primary prevention:

2.1.1 Communication for Behavior Change

- Increased awareness and knowledge of HCV transmission and prevention and control among the general population
- Provide specific messages to increase awareness and knowledge of HCV 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 HCV transmission.
- 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)
- 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 persons
2.1.3 Prevention of HCV transmission 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

2.1.4 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, the person should be retested for HCV 6 months’ post-exposure 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.
- No HCV infection vaccine is available yet.

2.2 Secondary and Tertiary Prevention of HCV Infection

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

Early diagnosis helps infected people to take precautions to protect the liver from additional harm by abstaining from alcohol and tobacco consumption and avoiding certain toxic drugs.

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

Chapter 2 Summary: Prevention of HCV Infection

There is currently no vaccine against HCV infection. Primary prevention of hepatitis C infection focuses on reducing risk of exposure to virus through advocacy for increased awareness and behavior change at the community-level, healthcare facility-level and individual-level, particularly for high risk groups. In cases of suspected exposure to hepatitis C contaminated blood and bodily fluids, site of exposure should be washed. Early detection and appropriate treatment for cure are essential for prevention of progression of HCV infection towards advanced liver disease.
Chapter III: Screening and Diagnosis of HCV Infection

3.1 Screening and Diagnosis of HCV Infection

Screening for HCV infection is done using either ELISA-based HCV serological testing or Rapid Diagnostic Tests (RDTs). If positive, a NAT for HCV RNA assay is used to confirm chronic HCV infection. Anti-HCV is generally not detectable in patients with initial signs or symptoms of hepatitis C and generally develops between 2 and 8 weeks after evidence of liver injury. Some persons may not test positive for 6-9 months after onset of illness.

All patients who screen positive for HCV antibody should also be screened for HBV and HIV infections.

Hepatitis C viremia may be detected by RT-PCR within 4-8 days after infection.

- In Rwanda, the screening of HCV is done by detecting the presence of HCV antibody (ELISA or Rapid Test)
- If HCV Ab is positive and confirmed with a positive HCV RNA test, the patient is confirmed to have HCV chronic infection and should be evaluated for treatment.
- If HCV RNA test is negative, the patient will be informed that the infection has been cleared and will receive appropriate counseling for prevention (Figure 7).

![Figure 6: Algorithm for screening and diagnosis of HCV infection](image-url)
3.2 Who should be screened?

Anybody seeking HCV screening should be offered the service. However, high risk groups cited in prevention section and patients with unexplained abnormal liver function are priority for HCV screening. It is not recommended by WHO to routinely screen pregnant women for HCV as they cannot be treated during pregnancy. Treatment for HCV (DAAs) is contraindicated during pregnancy.

Chapter 3 Summary: Screening and Diagnosis of HCV Infection

It is recommended that everyone should be screened although priority is given to high risk populations such as healthcare providers, HIV-infected populations, prisoners, key populations and patients with unexplained abnormal liver function. It is not recommended by WHO to routinely screen pregnant women as they cannot be treated during pregnancy.

Screening for hepatitis C is done through assessing the presence of anti-HCV using either ELISA test or rapid diagnostic tests (RDTs) and a confirmatory HCV RNA test.
Chapter IV: Treatment of HCV Infection

4.1 Initial Evaluation of HCV-infected Patients

Patients with chronic HCV infection should undergo thorough history and physical evaluation including risk factors & family history, extra-hepatic manifestations (ex. Skin rash, vasculitis) and co-morbidities. Tests to rule out viral co-infections such as HIV and HBV are mandatory.

Patient history and physical evaluation should be followed by complementary investigations for chronic HCV that includes:

- Aminotransferase/platelet ratio index (APRI) score
- ALT/ASAT
- Hematology (hemoglobin, platelets and leucocytes including differential count)
- Ultrasound when ascites decompensation is suspected
- Alpha-fetoprotein (AFP) when possible, in cirrhotic patients (APRI >2.0) with suspicion of HCC
- Endoscopy for esophageal varices in cirrhotic patients with platelets < 150x10^9/L when possible
- In addition, when available, elastography (fibroscan) should be considered for evaluation of liver fibrosis/ cirrhosis instead of liver biopsy, which is an invasive method.

APRI Score and Liver Fibrosis Assessment Formula

\[
\text{APRI} = \frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}} \times 100
\]

Platelets Count (109)/L

\[
\text{NB: In this formula, 3 zeros in platelets count are chopped off.}
\]

\[
\text{Example, if you have 137,000 platelets, you only consider 137}
\]

An online calculator can be found at:
http://www.hepatitisc.uw.edu/page/clinical-calculators/apri
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**Table 5: Interpretation of Aminotransferase Platelet Ratio Index (APRI)**

<table>
<thead>
<tr>
<th>APRI Value</th>
<th>Interpretation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2.0</td>
<td>High Probability of advanced fibrosis / cirrhosis (94%)</td>
<td>Determine whether compensated or decompensated and refer to care and treatment as appropriate</td>
</tr>
<tr>
<td>≤2.0</td>
<td>Low risk of advanced fibrosis</td>
<td>Treat all</td>
</tr>
</tbody>
</table>

---

**Figure 7: HCV Diagnosis and Treatment Algorithm**

[Diagram of HCV diagnosis and treatment algorithm]

*When APRI>2: consider additional interventions such as endoscopy, HCC screening, liver ultrasound or refer to a specialist

**Refer to specialist in complicated cases such as decompensated cirrhosis, children and co-infection of HCV&HBV
4.2 Treatment of HCV Mono-infection 17,23

4.2.1 Summary of HCV Treatment Recommendations and Indications
The goal of the treatment is to eradicate the virus, prevent liver cirrhosis and its complications including hepatocellular carcinoma (HCC) 17.
All patients with detectable HCV RNA viral load should be initiated on treatment with Direct Acting Antivirals (DAAs). Current treatment with DAAs is contraindicated in pregnant women and in children under 12 years old or less than 35 kg of weight. Recommended treatments are the following:

1) Children aged < 12 years
WHO recommends deferring treatment until 12 years are completed, as DAAs are contraindicated in this age category. Exceptionally, treatment with interferon + Ribavirin may be considered for children with genotype 2 or 3 infection with severe liver disease. These include children at higher risk of progressive liver disease such as with HIV-coinfection, thalassemia major and survivors of childhood cancer.

2) Adolescent aged 12 - 17 years or weighing 35 kg and above
   o Non cirrhotic and treatment naïve patients:
     • Sofosbuvir + Ledipasvir (400mg/90mg, OD) for 12 weeks in genotypes 1,4,5 and 6;
     • Sofosbuvir + Ribavirin for 12 weeks in genotype 2;
     • Sofosbuvir + Ribavirin for 24 weeks in genotype 3.
   o Cirrhotic and/or treatment experienced patients:
     • Sofosbuvir + Ledipasvir (400mg/90mg, OD) for 24 weeks in genotypes 1,4,5 and 6;
     • Sofosbuvir + Ribavirin for 24 weeks in genotype 2;
     • Sofosbuvir + Ribavirin for 24 weeks in genotype 3.

Note: Recommended treatment for adolescents aged 12-17 years is Sofosbuvir + Ledipasvir (Harvoni) based on its safety. This treatment with Harvoni can also be used for adults aged 18 years and above when there is no pangenotypic treatment. Pangenotypic treatments (Sofosbuvir + Daclatasvir; Sofosbuvir + Velpatasvir; Glecaprevir + Pibrentasvir) are recommended for patients aged 18 years and above.
3) Adults aged 18 years and above

For this category, *pangenotypic treatments are recommended as follows:

- **Non cirrhotic and treatment naïve patients:**
  - **Sofosbuvir + Daclatasvir; (400mg/60,30,90mg; OD); 12 weeks**
  - Sofosbuvir + Velpatasvir (400mg/100mg, OD); 12 weeks
  - Glecaprevir + Pibrentasvir (100mg/40mg, 3x/day); 8 weeks

- **Compensated cirrhotic and/or treatment experienced:**
  - **Sofosbuvir + Daclatasvir; (400mg/60,30,90mg; OD); 24 weeks**
    (12 weeks may be considered when the country prevalence of genotype 3 is < 5%).
  - Sofosbuvir + Velpatasvir (400mg/100mg, OD), 12 weeks
  - Glecaprevir + Pibrentasvir (100mg/40mg, 3x/day), 12 weeks
    (16 weeks are required when it is genotype 3 in treatment-experienced patients especially with interferon and/or ribavirin)

* A treatment with Harvoni can also be used for adults aged 18 years and above when the above pangenotypic treatments are not available.

**In case of HCV–HIV co-infected patients on treatment with Efavirenz based regimen, Daclatasvir dosing should be increased to 90mg daily and in case of co-administration with Protease inhibitor boosted with Ritonavir, Daclatasvir should be reduced to 30mg daily.**

- **Patients with Decompensated Cirrhosis**
  Diagnosis of decompensated liver disease is based on both laboratory and clinical assessment. A proportion of persons with decompensated liver disease will deteriorate on treatment and currently there are no predictors to identify these persons. Patients with decompensated cirrhosis are clinically complex and require close monitoring and long-term follow-up. These patients should be managed by specialist physicians. Sofosbuvir + Daclatasvir and Sofosbuvir + Velpatasvir have been studied in persons with decompensated cirrhosis and their use has been demonstrated to be generally safe and effective. In contrast, regimens that contain an HCV protease inhibitor (eg. Glecaprevir+Pibrentasvir) are not approved for use in persons with decompensated cirrhosis. The following treatment may be prescribed:¹⁸,²³
• Patients who are ribavirin-eligible (Hb>10g/dL): 12 weeks of either SOF+LDV or SOF+DCV or SOF+VEL + weight based ribavirin (1000-1200mg) Patients who are ribavirin-ineligible (Hb<10g/dL): 24 weeks of SOF+LDV, SOF+DCV, SOF+VEL

• Option for liver transplantation may be considered when possible.

Table 6: Administration of weight-based Ribavirin in adults

<table>
<thead>
<tr>
<th>Adult weight</th>
<th>Ribavirin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤75 kg</td>
<td>1000mg divided doses: 600mg (am) and 400mg (pm)</td>
</tr>
<tr>
<td>&gt;75 kg</td>
<td>1200mg divided doses: 600mg (am and pm)</td>
</tr>
</tbody>
</table>

4.2.2 Education and Preparation for HCV Treatment

Life style of patients is critical to the success of patient management. Patients should receive guidance on the following:

○ Length of treatment and potential side effects
○ The importance of treatment adherence for cure
○ Importance of SVR 12 to determine cure
○ Risk factors that can accelerate progression of liver damage include alcohol, substance abuse, obesity etc.
○ Advice on balanced diet and physical activity
○ Potential for re-infection after successful cure

4.2.3 Common Side Effects of Hepatitis C Antiviral Agents

Although DAAs are generally well-tolerated, the following side-effects detailed in Table 8 have been reported:

Table 7: DAAs and commonly reported side-effects

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir</td>
<td>Fatigue and headache</td>
</tr>
<tr>
<td>Ledipasvir</td>
<td>Fatigue, headache, insomnia, and nausea</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>Nausea, headache, fatigue</td>
</tr>
<tr>
<td>Velpatasvir</td>
<td>More common side effects include fatigue and headache, less common side effects include nausea, insomnia, diarrhea, rash and anemia</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Dose-dependent hemolytic anemia, headache, nausea insomnia and may cause dyspepsia and rash. Birth defects have been produced in animal experiments and contraception should be used during treatment and until 6 months after (female)/7 months after (males) end of treatment</td>
</tr>
</tbody>
</table>
4.3 Patient Follow-up

4.3.1 Patient Follow-up during Treatment

Patients will receive preferably 3 bottles of DAAs for the whole period of 12 weeks treatment to avoid any possible stock-out and consecutive interruption of treatment. However, if physicians judge necessary the monthly visit of a patient, for a need of a close follow-up, patients may be seen every 4 weeks for treatment monitoring. After treatment, patients should be seen at 12 weeks after end of treatment for SVR 12. In special cases, nurses can choose to refer patients to general practitioners (GPs) as-needed (ex. When patients report serious complications or side effects or if patients are from one of the special populations listed in Section 4.4). HIV-HCV co-infected patients will be followed-up by HIV nurses per HIV protocol. For patients on retreatment for 24 weeks, they should be seen at 12 weeks interval for general physical check-up as well as the assessment of adherence and side effects. No laboratory monitoring is required unless the patient is prescribed ribavirin in cases of cirrhosis or re-treatment after treatment failure. Ribavirin use requires more intensive monitoring for side-effects (Section 4.3.2).

On the day of the visit for (last) DAA pick-up as applicable, patients should be given an appointment for VL testing to evaluate treatment response (SVR12) 12 weeks after completing treatment course. Patient should be informed to return for VL testing at 12 weeks after last day of treatment course.

SVR12 results should be returned to prescribers for result interpretation. Patients should return to prescribing physician to be informed of results.
Undetectable HCV RNA levels 12 weeks or longer after end of treatment indicates treatment success.

4.3.2 Follow-Up of Patients on Ribavirin

Severe hemolytic anemia may occur in patients using Ribavirin-based regimens. When using Ribavirin, careful monitoring of hemoglobin (Hb) should be done. Hb levels need to be assessed before starting therapy and then at 2 and 4 weeks after therapy initiation.

- Start Ribavirin only if Hb>10g/dL
- If Hb<10g/dL, reduce Ribavirin by 200mg each week until Hb ≥ 10g/dL
- If Hb ≤ 8g/dL, stop Ribavirin for 2 weeks then resume at 600mg daily (or 200mg lower than last administered dose) and monitor Hb weekly
- When Hb <10g/dL, monitor Hb weekly
In cases of renal failure in patients using Ribavirin, the following is recommended:

- If CrCl 30-50 mL/min use 200mg alternating with 400mg daily
- If CrCl <30 mL/min or hemodialysis use 200mg daily

4.3.3 Treatment Adherence

Patient adherence to prescribed treatment regimen is crucial to successfully achieve a viral suppression. Prior to treatment initiation, physicians and/or nurses should provide adherence counselling including basic information on the benefits and side effects of antiviral medications, how the medications should be taken and the importance of not missing any dose.

- Pre-treatment adherence counselling
- Monitoring adherence during treatment
- Managing side effects during treatment

The following factors are known to improve adherence:

- Increased availability of treatment and reduced stock-outs
- Patient cards where appointment dates are pre-specified, including SVR date
- Adherence counselling pre-treatment and during treatment
- Adherence monitoring during treatment
- Managing side effects during treatment
- Individual patients, family and other treatment supporters
- Drug regimen simplicity or shorter duration of therapy when possible

In cases of missed doses or treatment interruption, healthcare providers should provide enhanced adherence support till the end of treatment course. SVR12 should be assessed as usual and decision guided by result. In complicated cases of non-adherence, refer to specialist.

4.3.5 Patient Visit Post-SVR

Upon availability of SVR results, patients should return to monitoring Physician to interpret SVR results. Physicians should interpret SVR results and discuss patient compliance.

4.3.5.1 Cured (VL suppressed) Patients

Remind patients that they can still be re-infected with HCV and review patient understanding of routes of HCV transmission while discussing methods to avoid risky behavior and lifestyle. For patients who are cured with no evidence of cirrhosis (APRI <1.0), the recommended follow-up is the same as if they were never infected with HCV.
For patients with moderate fibrosis (APRI 1.0-2.0) closer follow-up may be warranted. Patients with a high likelihood of cirrhosis (APRI>2.0) should be assessed for ongoing risk of HCC.

Assessment of reinfection is recommended only if the patient has ongoing risk for HCV infection. Quantitative HCV RNA assay is needed to assess reinfection rather than ant-HCV serology test.

Curing HCV infection for patients with cirrhosis does not cure patient’s cirrhotic status. Patients who are cured with evidence of liver cirrhosis have a persistent risk of hepatocellular carcinoma. They should be followed up every six months with lab tests for liver enzymes, ultrasonography and AFP for HCC monitoring. Monitoring for esophageal varices using endoscopy should be conducted at least once in a lifetime for patients with cirrhosis and platelets <150 x 10^9 /L. Further follow-up of patients found to have varices is at the discretion of the specialist.

4.3.5.2 Not Cured (VL not suppressed) Patients

If patient is not cured (VL not suppressed), retreatment using highly effective drugs should be done and monitoring GPs should refer to specialists for further evaluation as necessary. Follow-up assessments should be planned.

Liver disease progression should be assessed every 6 to 12 months through hepatic function panel and complete blood count (CBC). For patients with advanced fibrosis, HCC screening should be conducted every 6 months. Monitoring for esophageal varices should be conducted for patients with cirrhosis.

4.4 HCV Treatment in Special Populations

4.4.1 HIV-HCV Co-Infection

4.4.1.1 Overview of HIV-HCV Co-Infection

Co-infection with HIV adversely affects the course of HCV infection. Co-infected persons have a risk of accelerated progression to compensated and decompensated cirrhosis and HCC compared to HCV-monoinfected persons, especially those with advanced immunodeficiency (CD4 count <200 cells/mm^3)^2. However, indications for treatment in HCV/HIV co-infected patients are identical to HCV-mono-infected patients and co-infected patients have the same likelihood of achieving SVR as mono-infected patients. The following is recommended for patients co-infected with HIV-HCV:
HIV-infected patients should be screened for hepatitis C virus (HCV) infection, preferably before starting antiretroviral therapy (ART).

Treat all HIV/HCV co-infected patients for both HIV and HCV

When treatment for both HIV and HCV is indicated, consider drug-drug interactions and overlapping toxicities

In ART naive patients with CD4 counts >500 cells/mm³, if there is concern of drug-drug interaction, consider completing HCV treatment prior to ART initiation

In patients with lower CD4 counts < 200 cells/mm³ with no advanced liver disease, it is recommended to initiate ART and delay HCV therapy until CD4 counts increase.

For patients with CD4 count between 200 – 500 cells/mm³ the time to initiate treatment will be situational.

4.4.1.2 Drug combinations of ART and DAAs

Persons with HIV require special consideration regarding the selection of a DAA regimen. Detailed recommendations on specific ART and DAA combinations can be found in Table 9.

**Sofosbuvir**

The safety profile in HCV/HIV-1 co-infected subjects treated with Sofosbuvir is similar to that observed in HCV-mono-infected subjects. However, sofosbuvir-based regimens should not be used with tipranavir/ritonavir. Elevated total bilirubin (grade 3 or 4) occurs extremely commonly in persons treated with Sofosbuvir and Atazanavir as part of the antiretroviral regimen.

**Sofosbuvir (400mg) + Ledispavir (90mg)**

Renal function should be monitored when SOF+LDV is given with TDF/TAF because this combination increases plasma levels of TDF/TAF. SOF+LDV can be used in patients with eGFR >30 ml/min.

**Daclatasvir**

- Increase daclatasvir dosage to 90mg per day when co-administered with NNRTI’s Efavirenz, Nevirapine or Etravirine
- Decrease daclatasvir dosage to 30mg per day when co-administered with Atazanavir+Ritonavir
- Do Not co-administer daclatasvir with Rifampin
Sofosbuvir (400mg) + Velpatasvir (100mg)
Renal function should be monitored when SOF+VEL is used in combination with TDF/TAF because this combination increases plasma levels of TDF/TAF. SOF+VEL can be used in patients with Egfr>30ml/min. SOF+VEL should not be co-administered with EFV, Etravirine and Nevirapine.

Glecaprevir (100mg) + Pibrentasvir (40mg)
This treatment cannot be used in combination with ATZ/r (Atanazavir/ Ritonavir)

Summary of actions not recommended in HIV/HCV co-infected patients:
- Antiretroviral treatment interruption to allow HCV therapy
- Sofosbuvir+velpatasvir should not be used with efavirenz, etravirine, or nevirapine
- Sofosbuvir-based regimens should not be used with tipranavir/ritonavir
- Ribavirin should not be used with didanosine, stavudine, or zidovudine

Table 8: Effect of drug combinations and recommended actions between ARTs and DAAs.18, 23
4.4.2 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\textsuperscript{21}. Persons with compensated cirrhosis have the least time available for treatment, the most to lose and much to gain from achieving SVR. HCV treatment is ideally commenced before the onset of decompensated disease.

Cirrhotic patients with liver failure (cirrhosis with jaundice, ascites, encephalopathy, esophageal varices bleeding) should be reviewed by a doctor for specific treatment.

4.4.3 Hepatitis C in pregnant women

There is a risk of mother-to-child transmission (MTCT) of HCV of roughly 5% in HCV mono-infected women and 10% in HIV/HCV co-infected women. There are currently no interventions available to decrease MTCT of HCV. Women of child-bearing age already infected with HCV should be advised to delay pregnancy until treated and cured of HCV\textsuperscript{18}. Pregnant women can be screened for HCV infection during antenatal visits. Pregnant women who screen negative for HCV should be counselled of prevention strategies against hepatitis C infection during the antenatal period. For pregnant women who screen positive, a confirmatory viral load will be done. If the woman is confirmed positive for chronic HCV infection, treatment will be delayed until post-partum and post-breastfeeding due to concerns with drug safety. If cirrhotic, counselling should be done to inform on increased risk of adverse maternal and perinatal outcomes including preeclampsia, cesarean section, hemorrhagic complication, preterm delivery, low birth weight and mother or neonatal death\textsuperscript{18}.

Breastfeeding is not contraindicated in women with HCV infection, except when the mother has cracked, damaged, or bleeding nipples, or in the context of HIV coinfection\textsuperscript{18}. Ribavirin is contraindicated during pregnancy and those with child-bearing potential unless with contraception during and 6 months after termination of drug-use\textsuperscript{18}.

4.4.4 Hepatitis C in children and adolescents

4.4.4.1 Diagnosis

Hepatitis C maternal antibodies can be present in the child till 18 months. Hepatitis C is diagnosed in children with a positive anti-HCV test starting from 18 months and HCV RNA confirmation 3 months after positive anti-HCV test. Upon positive lab tests, children will be assessed for progression of liver disease (similar to assessment in adults).
4.4.4.2 Treatment of Children without Decompensated Cirrhosis

Children aged 12 years and above
Treatment options for children depend on age, weight in addition to cirrhotic status and whether or not the child has previous treatment. Children confirmed with chronic HCV infection who are over 12 years of age and weigh over 35kg and do not have decompensated cirrhosis are eligible for treatment as detailed below.

Children Aged < 12 years
Children under 12 years of age confirmed with chronic HCV infection are currently not eligible for DAAs due to concerns with drug safety. Children in this age category who are not cirrhotic should be followed-up until he/she is 12 years of age and 35 kg to be initiated on DAAs. As said above under 4.3., treatment with interferon + ribavirin may be considered only in some special cases of severe and progressive liver disease.

4.4.4.3 Treatment of Children with Decompensated Cirrhosis
- General Practitioners to refer such cases to specialists

4.4.4.4 Weight-Based Ribavirin in Children
When Ribavirin is indicated in treatment such as with GT-2 and GT-3, daily dosage of Ribavirin should be administered orally in two divided doses with food. The following table details recommended dosing for Ribavirin in patients 12 years of age and older or weighing at least 35 kg.

Table 9: Daily dosage of Ribavirin for children based on body weight

<table>
<thead>
<tr>
<th>Body Weight kg</th>
<th>Ribavirin Daily Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 47 kg</td>
<td>15 mg/kg/day</td>
</tr>
<tr>
<td>47-49</td>
<td>600 mg/day</td>
</tr>
<tr>
<td>50-65</td>
<td>800 mg/day</td>
</tr>
<tr>
<td>66-80</td>
<td>1000 mg/day</td>
</tr>
<tr>
<td>&gt;80</td>
<td>1200 mg/day</td>
</tr>
</tbody>
</table>
4.4.5 Additional Considerations
Management of HCV in children and adolescents should involve their parents or caregivers. Parents should be counselled on HCV transmission in order to minimize stigmatization of the child and precautions to minimize HCV transmission. Adolescent patients undergoing treatment should be monitored by pediatricians or physicians with expertise in managing and monitoring HCV in pediatric subpopulations.

4.4.5 HBV-HCV Co-Infection
HBV and HCV share similar modes of transmission with the possibility of co-infection. In co-infected patients not yet eligible for HBV treatment, DAA treatment should be initiated without delay. There have been reports of HBV reactivation leading to potentially severe acute/fulminant liver disease among co-infected patients who initiated DAA treatment without co-administration of TDF/TAF. Co-infected patients initiated on DAAs but not yet on TDF/TAF, should be continuously monitored with HBV DNA VL at least every 3 months especially at the beginning and the end of HCV treatment, and 3 months after end of HCV treatment. If HBV DNA increases 10-fold or >1000UI/mL in addition to baseline HBV DNA VL, TDF/TAF treatment should be initiated and patients have to be monitored with lab tests relevant to liver function (AST, ALT etc.)\(^\text{19,23}\).

HBV-HCV co-infected patients already on HBV treatment who are planning to initiate DAA treatment should continue HBV treatment and the treatment can be co-administered for HBV and HCV.

HBV-HCV co-infected patients eligible to both HBV and HCV treatments, HBV treatment should be started before HCV treatment to avoid HBV reactivation leading to potentially severe acute/fulminant liver disease among co-infected patients. HCV treatment can be started 4 weeks after initiation of HBV treatment\(^\text{19,23}\).

4.4.6 Patients with Renal Impairment
Caution should be taken when administering ribavirin to patients with renal impairment. Ribavirin is predominantly excreted by the kidneys and the drug should normally not be used in patients with a creatinine clearance <60mL/min\(^2\). On an individual basis, ribavirin may be 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.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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.

The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus. These guidelines would not have been finalized without the usual 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 hepatitis technical working group and respective organizations that contributed to the development of this document.

___________________________
Dr Diane GASHUMBA
Minister of Health

### Table 10: Dose adjustments and monitoring of DAA-use by stage of Chronic Kidney Disease (CKD)

<table>
<thead>
<tr>
<th>Chronic kidney disease stage (CKD)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD 1,2 &amp; 3 (eGFR&gt;30ml/min)</td>
<td>No dose adjustment is required when using:</td>
</tr>
<tr>
<td></td>
<td>• Fixed-dose combination of ledipasvir (90 mg) + sofosbuvir (400 mg)</td>
</tr>
<tr>
<td></td>
<td>• Fixed-dose combination of sofosbuvir (400 mg) + velpatasvir (100 mg)</td>
</tr>
<tr>
<td></td>
<td>• Sofosbuvir (400 mg)</td>
</tr>
<tr>
<td></td>
<td>• Daclatasvir (60 mg)</td>
</tr>
<tr>
<td></td>
<td>Dose adjustment when using ribavirin:</td>
</tr>
<tr>
<td></td>
<td>• 400mg alternate with 200mg daily</td>
</tr>
<tr>
<td>CKD stage 4&amp;5 (eGFR&lt;30ml/min)</td>
<td>• Limited data on the use of sofosbuvir 400mg based regimen; use of sofosbuvir based regimen requires close monitoring</td>
</tr>
<tr>
<td></td>
<td>• Dose adjustment when using ribavirin: 20mg daily</td>
</tr>
</tbody>
</table>

### 4.4.7 TB and HCV Co-Infection

In patients co-infected with TB and HCV, it is recommended that TB should be treated before commencing therapy for HCV. The following table documents drug indications for uses of HCV DAAs with commonly used TB drugs.

Table 11: DDIs between commonly used TB drugs and DAAs

<table>
<thead>
<tr>
<th>INH</th>
<th>SOF</th>
<th>SOF+LDV</th>
<th>SOF+DCV</th>
<th>SOF+VEL</th>
<th>SOF+VEL+VOX</th>
<th>RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
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<tr>
<td>Pyrazinamid</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: [https://www.hep-druginteractions.org/](https://www.hep-druginteractions.org/)

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© Guidelines for HBV, HCV and STIs management
There is limited data on the co-management of persons co-infected with HCV, HIV and TB. Clinical judgement is needed in order to reduce additive side-effects, pill burden and drug-drug interactions.

4.5 Drug-drug Interactions (DDI)

Multiple drug use is at times common in patients initiating treatment on DAAs, so there is potential for drug-drug interaction. DAAs are metabolized by the Cytochrome P450 3A4 isoenzyme in the liver. Other drugs metabolized by this enzyme can either raise or lower the level of DAAs or be increased or decreased themselves by these interactions.

4.5.1 Warnings / Contraindications to Therapy

Sofosbuvir-based regimens (SOF+LDV, SOF+VEL) are contraindicated in patients receiving amiodarone who cannot switch therapies. Sofosbuvir should be used with caution in patients with severe renal impairment (eGFR <30mL/min) as safety of sofosbuvir-derived metabolites in patients with severe renal dysfunction is still being ascertained. Daclatasvir is contraindicated in patients taking rifampicins, phenytoin, or carbamazepine. Ribavirin is contraindicated in pregnant women, men whose partners are pregnant and patients with hemoglobinopathies.

Table 12: Drugs contraindications/ warnings

<table>
<thead>
<tr>
<th>Drug Contraindications / warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sofosbuvir</strong></td>
</tr>
<tr>
<td>• Amiodarone co-administration</td>
</tr>
<tr>
<td>• Renal failure (eGFR &lt;30 mL/min/1.73 m2)</td>
</tr>
<tr>
<td><strong>Sofosbuvir + Ledipasvir</strong></td>
</tr>
<tr>
<td>• Amiodarone co-administration</td>
</tr>
<tr>
<td>• P-glycoprotein (gp) inducers</td>
</tr>
<tr>
<td>• Renal failure (eGFR &lt;30 mL/min/1.73 m2)</td>
</tr>
<tr>
<td><strong>Daclatasvir</strong></td>
</tr>
<tr>
<td>• Drugs inducing or inhibiting CYP3A</td>
</tr>
<tr>
<td><strong>Ribavirin</strong></td>
</tr>
<tr>
<td>• Pregnant women or men whose partners are pregnant</td>
</tr>
<tr>
<td>• Didanosine can result in life-threatening toxicity</td>
</tr>
<tr>
<td>• Azathioprine can cause myelotoxicity</td>
</tr>
<tr>
<td>• Caution with Stavudine, Zidovudine, Lamivudine</td>
</tr>
<tr>
<td><em>(Decreased antiretroviral activity)</em></td>
</tr>
</tbody>
</table>

In addition to the contraindications and warnings mentioned in section 4.5.1 and drug interactions between HIV ARTs in section 4.4.1.2, the following precautions should also be taken:
- Herbal supplement St. John’s wort is not recommended with Sofosbuvir
- Antiepileptics of carbamazepine, phenytoin, phenobarbital and oxcarbazepine cannot be used with DAAs
- If SOF+LDV is used with antacids, the two should be taken at least 4 hours apart
- It is not recommended to co-administer SOF+VEL to patients taking antacids
- Daclatasvir should be decreased to 30mg once daily when used with clarithromycin, itraconazole, ketoconazole and voriconazole
- Ribavirin is contraindicated during pregnancy and those with child-bearing potential unless with contraception during and 6 months after termination of drug-use
- Rifampin should not be co-administered with DAAs

An exhaustive list of DDIs can be found at http://www.hep-druginteractions.org. In doubt, please consult this database and a specialist.

4.6 Treatment Failure
4.6.1 Reasons for Treatment Failure
Treatment failure, defined as detectable HCV RNA 12 weeks after end of treatment, can occur due to the following reasons:
1. Patient non-adherence
2. Administration of regimen that was not preferred especially when treating with non-pan-genotypic drugs
3. Drug-drug interactions decreasing efficacy of DAAs (see section 4.5)
4. Drug resistance

4.6.2 Recommended Actions for Treatment Failure
In case of treatment failure, patients should be referred to a specialist. To date, the only highly effective recommended drug for treatment failure is SOF+VEL+VOX. When SOF+VEL+VOX is not available for retreatment, Specialists should reevaluate patient with relevant lab tests and can use the following treatment guiding principles:
- Addition of Ribavirin to failed treatment and possible extension of treatment duration to 24 weeks depending on specialist consultation.
- If no ribavirin available, the treatment duration after failure is also 24 weeks.
- Keep the same period of treatment as 12 weeks when using SOF+VEL+VOX. SOF+VEL+VOX cannot be used in cirrhotic patients with Child-Pugh Class B or C cirrhosis or with renal failure.
- Glecaprevir/ Pibrentasvir combination is effective for retreatment of patients that failed SOF based regimens and those who have failed treatment with either a protease inhibitor or an NS5A inhibitor (but not both). Treatment duration is 16 weeks.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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. The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected with the mentioned virus.

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Dr Diane GASHUMBA
Minister of Health

Table 13: DAA regimens and durations for re-treatment of patients who are non-cirrhotic or have compensated cirrhosis\textsuperscript{18}

<table>
<thead>
<tr>
<th>Regimen 1\textsuperscript{st} line</th>
<th>Duration 1\textsuperscript{st} line</th>
<th>Regimen 2\textsuperscript{nd} line</th>
<th>Duration 2\textsuperscript{nd} line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir 400mg OD + Ledipasvir 90mg OD</td>
<td>12 weeks</td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL +Ribavirin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF +LDV+Ribavirin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+DCV+Ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Sofosbuvir 400mg OD + Daclatasvir 60/30 mg OD</td>
<td>12 weeks</td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL+Ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+DCV+Ribavirin</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir 400mg OD + Velpatasvir 100mg OD</td>
<td>12 weeks</td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL + Ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Glicaprevir 100mg OD + Pibrentasvir 40 mg OD</td>
<td>8 weeks</td>
<td>Glicaprevir 100mg + Pibrentasvir 40 mg</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

Note:

- When SOF+VEL+VOX is not available, retreatment can be based on available treatment regimens with addition of ribavirin and the treatment has to be extended to 24 months to maximize the chances of cure as the longer the duration, the better the results.
- When no ribavirin available, retreatment can be based on available treatment regimens extended to 24 weeks. Example: A Patient who failed SOF+LDV for 12 weeks as initial treatment, can be given SOF+LDV or SOF+DCV or SOF+VEL for 24 weeks in the absence of ribavirin depending on the available regimen. However, a pan genotypic treatment is always preferred.

4.6.3 Drug Resistance

There is potential for drug resistance with DAAs. When physicians have exhausted all other options reasons for treatment failure, genetic sequencing for resistance testing can be done to select the most appropriate DAA for future therapy. This should be done only in consultation with an expert specialist.
Chapter 4 Summary: Management of People with Hepatitis C Infection

All patients with detectable HCV RNA viral load should be initiated on treatment with Directly Acting Antivirals (DAAs) unless they belong to special populations requiring additional considerations. Initial evaluation of patients chronically-infected with HCV include APRI score (Equation 1) to assess cirrhosis, ALAT/ASAT and hematology tests.

In Rwanda, general treatment for patients who are either non-cirrhotic/ cirrhotic and are treatment-naïve/experienced for DAAs would consist of a period of 8-24 week course using the following drugs:

<table>
<thead>
<tr>
<th>Regimen 1st line</th>
<th>Duration 1st line</th>
<th>Regimen 2nd line</th>
<th>Duration 2nd line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir 400mg OD + Ledipasvir 90mg OD</td>
<td>12 weeks</td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL+Ribavirin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+LDV+Ribavirin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+DCV+Ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Sofosbuvir 400mg OD + Daclatasvir 60/30 mg OD</td>
<td>12 weeks</td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL+Ribavirin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+DCV+Ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Sofosbuvir 400mg OD + Velpatasvir 100mg OD</td>
<td>12 weeks</td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL + Ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Glicaprevir 100mg OD+ Pibrentasvir 40 mg OD</td>
<td>8 weeks</td>
<td>Glicaprevir 100mg + Pibrentasvir 40 mg</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SOF+VEL+VOX</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

Patient Follow-Up during Treatment

Patients should be administered preferably a 12 weeks treatment at a visit and particularly be seen every month if there is a need for a close follow-up. An HCV RNA test no-sooner than 12-weeks after completion of treatment course is necessary to assess treatment success, defined by undetectable HCV RNA 12-weeks post-treatment. Patients on ribavirin involve more careful monitoring of hemoglobin levels. Treatment adherence is key to achieve a successful cure. Efforts such as adherence counselling prior to and during treatment and management of side effects of should be taken to improve adherence.
Patient Follow-Up Post-Treatment

There are no specific recommendations for long-term follow-up of non-cirrhotic patients who are cured from HCV infection. All patients with cirrhosis should be followed-up every six months for HCC monitoring regardless of whether or not they were cured. Patients who are not cured should be referred to a specialist.

Special Cases for Care and Treatment

Special care (Referral to specialists) should be taken when managing and treating the following patient groups as detailed in Part II Section 4.4 of the guidelines.

- Patients co-infected with HIV-HCV: are systematically treated although consideration should be given to avoid drug-drug interaction with HIV treatment
- Patients with decompensated cirrhosis: are clinically complex and require close monitoring and long-term follow-up
- Pregnant women: should delay treatment until post-breastfeeding
- Children and adolescents: Children older than 12 years and weighing over 35kg are eligible for DAA-treatment. Those who do not meet age and weight eligibility should be followed-up
- Patients co-infected with HBV-HCV: careful monitoring for severe acute/fulminant liver disease
- Patients with renal impairment
- Patients co-infected with TB-HCV

Drug-Drug Interactions (DDIs)

Multiple drug use is at times common in patients initiating treatment on DAAs, so there is potential for drug-drug interaction. Co-administration of the following with DAAs should be given special care:

- ARTs
- Amiodarone
- Rifampin
- Antacids
- Anti-epileptics
KEY MESSAGE FOR HCV MANAGEMENT

1. HCV is screened by detecting the presence of HCV Ab (ELISA or Rapid Test)

2. Diagnosis of chronic HCV is defined as detectable HCV RNA viral load

3. All patients diagnosed with chronic HCV should be initiated on treatment with DAAs unless they are part of special population groups requiring additional considerations or monitoring by specialists.

4. DAAs are generally well-tolerated with few side effects

5. Patients should be followed up as needed by health facilities during therapy.

6. Patients who are cured with evidence of liver cirrhosis have a risk of HCC; they should be followed up every 6 months with lab tests for liver enzymes.

7. If a patient is not cured, he/she has to be retreated and monitoring GPs should refer the patient to specialists for further evaluation.

8. HIV-infected patients have increased risk of accelerated progression to compensated and decompensated cirrhosis and HCC

9. Treatment for pregnant women confirmed HCV RNA positive will be delayed until post-breastfeeding.

10. HCV treatment with DAAs is recommended to children confirmed with chronic HCV infection who are above 12 years of age, weigh at least 35kg and do not have decompensated cirrhosis. Children under 12 years infected by chronic HCV are advised to wait until they have 12 years. Exceptionally, interferon + ribavirin regimen may be considered when there is a progressive and severe liver disease.
PART III: VIRAL HEPATITIS
PROGRAM IMPLEMENTATION
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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.

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___________________________
Dr Diane GASHUMBA
Minister of Health
Chapter I: 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 persons with chronic hepatitis B and C infections in Rwanda depends 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), viral hepatitis program will continue to be implemented following the minimum package of services per level of implementation.

In general, viral hepatitis services are composed of prevention including all sensitization methods to raise awareness and hepatitis related skills, screening and diagnosis of both HBV and HCV based on capacity but also care, treatment and patient follow-up including specific counseling and timely referral of complicated cases to higher level facilities according to the national guidelines.

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

The new guidelines will introduce task-shifting where general practitioners (GPs) are authorized to and trained to prescribe both HBV and HCV treatment medication. Specialists will be available to provide supervision and guidance as needed.

Chapter II: Minimum Package of Services

Blood Borne Viral Hepatitis 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.

Chapter III: General Practitioner (GP) Referral

Complicated or special cases that cannot be treated or managed by GPs should always be referred to specialists.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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. The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus. These guidelines would not have been finalized without the usual 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 hepatitis technical working group and respective organizations that contributed to the development of this document.

Table 14: Minimum package for Viral Hepatitis B&C Services per Level of Health Facility

<table>
<thead>
<tr>
<th>Level/Provider</th>
<th>Prevention</th>
<th>Laboratory</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Community</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| - CHWs         | - Prevention message  
- Provide information to the community | - Provide information to the community | - Program adherence support  
- Provide information to the community |
| **Health Center** |            |            |           |
| - Nurse        | - Prevention message  
- Vaccination of new born  
- Adults vaccination  
- Post exposure prophylaxis  
- Capacity building of CHWs | - Rapid tests for screening  
- Liver function tests  
- Renal function tests  
- Hematology | - Clinical assessment for cirrhosis  
- Assess eligibility criteria for HBV using available capacities  
- Counselling (adherence, lifestyle)  
- Initiate HBV and HCV treatment for simple cases  
- Follow up of patients on HBV and HCV treatment  
- Refer complicated cases to the next level as appropriate |
| - Laboratory Technician |            |            |           |
| - Physician | - Prevention message  
- Vaccination of new born  
- Adults vaccination  
- Post exposure prophylaxis  
- Supervision and clinical mentorship of Health centers | - Rapid tests for screening  
- Liver function tests  
- Renal function tests  
- Hematology  
- Capacity building of Lab technicians at health Center Level (Training, Mentorship) | - Clinical assessment for cirrhosis  
- Assess eligibility criteria for HBV using available capacities  
- Counselling (adherence, lifestyle)  
- Initiate HBV for intermediary complicated cases  
- Initiate HCV treatment for simple cases  
- Refer complicated cases to the next level as appropriate  
- Follow up of patients on HBV and HCV treatment  
- Capacity building of Nurses at Health Center Level (Training, Mentorship) |
| **District Hospital** |            |            |           |
| - General Practitioner | - Prevention message  
- Vaccination of new born  
- Adults vaccination  
- Post exposure prophylaxis  
- Supervision and clinical mentorship of Health centers | - Rapid tests for screening  
- Liver function tests  
- Renal function tests  
- Hematology  
- Capacity building of Lab technicians at health Center Level (Training, Mentorship) | - Clinical assessment for cirrhosis  
- Assess eligibility criteria for HBV using available capacities  
- Counselling (adherence, lifestyle)  
- Initiate HBV for intermediary complicated cases  
- Initiate HCV treatment for simple cases  
- Refer complicated cases to the next level as appropriate  
- Follow up of patients on HBV and HCV treatment  
- Capacity building of Nurses at Health Center Level (Training, Mentorship) |
| - Nurse        |            |            |           |
| - Laboratory Technician | - Prevention message  
- Vaccination of new born  
- Adults vaccination  
- Post exposure prophylaxis  
- Capacity building of medical at District Hospitals (Training, Mentorship, Supervision) | - Rapid tests for screening  
- Liver function tests  
- Renal function tests  
- Hematology  
- ELISA Tests  
- Viral Load Monitoring  
- Capacity building of Lab technicians at District Hospitals (Training, Mentorship, Supervision) | - Assess eligibility criteria for HBV using available capacities  
- Counselling (adherence, lifestyle)  
- Initiate HBV treatment for complicated cases  
- Initiate HCV treatment for simple and complicated cases  
- Follow up of patients on HBV and HCV treatment  
- Capacity building of medical personnel at District Hospitals (Training, Mentorship, Supervision) |
| - Counselor    |            |            |           |
| - Nutritionist |            |            |           |
PART IV: SEXUALLY TRANSMITTED INFECTIONS MANAGEMENT
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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.

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Dr Diane GASHUMBA
Minister of Health
Chapter I. Generalities on Sexually Transmitted Infections (STIs)

1.1. Principles of the care of Sexually Transmitted Infections (STIs) is based on the following principles:
   • Integration of STI control activities in the minimum activity package of health services;
   • Advocacy and mobilization of resources;
   • Implementation of multi-sector participation;
   • Mobilization and education of the community and high-risk groups about signs and symptoms of STIs, the modes of transmission, prevention, early consultation for diagnosis and treatment;

1.2. Definitions of terms and concepts

Sexually transmitted infections (STIs): Infections that are due to microbial agents (bacteria, virus, parasites, fungi), which are transmitted exclusively or mainly through sexual relations. Note that microbial agents are often associated among themselves and infections become mixed.

Index client (case): STI client treated in the health system from which we search for one or several partners.

Clients-contacts (or sexual partners): Persons who will have or had sexual relations with the Index client

Search for partners: Methodological investigation based on responses from the index client that enables the census and the treatment of contact-clients.

Sex worker: Any professional activity that consists of satisfying sexual needs of another person in exchange of material or financial goods.

Paedophilia: Any sexual activity carried out on children by adults.

MSM (Pederast/homosexual): Any male person who engages in sexual activities with other people of the same sex

Key population: Defined by UNAIDS as people who inject drugs, gay men (MSM) and other men who have sex with women (MSM, bisexual), transgender persons and sex workers. Also referred to as most-at-risk populations

Core group (group of the transmission): Group of people in a limited population who maintain and perpetuate the propagation of STI within the community (Ex. Sex workers).

Bridging population: People having sexual relations with the core group as well as the general population: i.e. the clients of sex workers.

Genital tracts infections (GTI): Infection of the genital organs including STIs and those not always transmitted by sexual means.
Table 15: STIs infections and responsible agents

<table>
<thead>
<tr>
<th>Name of the infection</th>
<th>Name of the micro-organism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STIs due to bacteria</strong></td>
<td></td>
</tr>
<tr>
<td>Gonococcus</td>
<td>Neisseria gonorrhoea</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Treponema pallidum</td>
</tr>
<tr>
<td>Wet Chancre</td>
<td>Bacilli of Ducrey</td>
</tr>
<tr>
<td>Venereal Lymphogranulomatosis (VLG) or the disease of Nicolas Favre</td>
<td>Chlamydia trachomatis</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Chlamydia trachomatis</td>
</tr>
<tr>
<td>Mycoplasmosis</td>
<td>Ureaplasma urealyticum and Mycoplasma hominis</td>
</tr>
<tr>
<td>Donovansosis</td>
<td>Calymmatobacterium granulomatis</td>
</tr>
<tr>
<td>Bacterial Vaginosis</td>
<td>Anaerobic bacteria</td>
</tr>
<tr>
<td><strong>STIs due to fungi (mycosis)</strong></td>
<td></td>
</tr>
<tr>
<td>Candida</td>
<td>Candida albicans</td>
</tr>
<tr>
<td><strong>STIs due to other parasites</strong></td>
<td></td>
</tr>
<tr>
<td>Scabies</td>
<td>Sarcoptes scabiei hominis</td>
</tr>
<tr>
<td>Phtiriasis</td>
<td>Phtirius inguinalis</td>
</tr>
<tr>
<td><strong>STIs due to Protozoa</strong></td>
<td></td>
</tr>
<tr>
<td>Trichommonas</td>
<td>Trichomones vaginalis</td>
</tr>
<tr>
<td><strong>STIs due to virus</strong></td>
<td></td>
</tr>
<tr>
<td>HIV infection</td>
<td>Human Immuno-deficiency virus HIV 1 and HIV 2</td>
</tr>
<tr>
<td>Genital Herpes</td>
<td>Herpes virus simplex type 2</td>
</tr>
<tr>
<td>Condyloma acuminate( or Venereal Vegetations (VV))</td>
<td>Human Papillomavirus</td>
</tr>
<tr>
<td>Viral Hepatitis B</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>Viral Hepatitis C</td>
<td>Hepatitis C Virus</td>
</tr>
</tbody>
</table>

1.3. Risk Factors

1.3.1. Biological Factors

- **Age:** Rates of STIs tend to peak between 15 and 24 years of age and then decline. Up until puberty, children do not suffer from STIs apart from genital syphilis, neonatal conjunctivitis, and HIV infection transmitted from mother to child.
- **Sex:** STIs are more frequent among women than among men due to several factors:
1) precocity of sexual relations in girls where girls are more likely to have sexual relations with older partners at higher risk for infection; 2) biological vulnerability due to immaturity of genital organs in adolescence; 3) larger area of exposure of the vagina; 4) Shorter length of female urethra compared to males.

- **Others:** Weak immunity status and non-circumcision in males are additional risk factors

1.3.2. **Socioeconomic Factors**
- Poverty
- Wars
- Displacement of populations
- Professions involving movement (Ex. internal and external land migrants, long-distance truck drivers, army, police, seasonal workers, miners or gold diggers, itinerant traders, tourists)
- Ignorance of the mode of transmission of STI
- Marital situations including forced and premature marriage
- Socio-economic dependence of the woman and lack of sexual control;
- Early debut sexual intercourse

1.3.3. **Behavioral Factors**
- Unprotected sexual relations
- Sexual intercourse with multiple partners;
- Unprotected sex with sex workers;
- Sexual relations with casual partners;
- High risk sexual practices (anal, oral, homosexuality, bisexuality etc.);
- Auto-medication;
- Drug use and alcohol abuse.

1.3.4. **Cultural Factors**
- Taboos linked to sex

1.4. **Relationship between HIV and other STIs**
Several epidemiological and biological studies provide evidence of a complex interaction between HIV and other STIs through the following mechanisms:
- STIs facilitate the transmission of HIV
- The presence of HIV may make the persons more susceptible to STIs
- The presence of HIV aggravates certain STIs and increases their resistance to treatment
Chapter II. Prevention of STIs

2.1 Strategies
The prevention and the control of STIs are based especially on five major strategies:

1. **Education and counselling** of high risk persons on changing their sexual behavior;
2. The **identification** of infected persons with clinical signs (symptomatic) or without clinical signs (asymptomatic) that should consult services in charge of diagnosing and treating STIs;
3. Efficient and **early diagnosis and treatment** of persons infected by STIs;
4. Evaluation, treatment, and counselling of **partners of persons** infected by STIs;
5. **Vaccination** of girls aged between 11 and 15 of HPV infection, especially before they start sex.

2.2 Primary Prevention
Primary prevention involves activities that will reduce the risk of infection through reducing high risk sexual activities or interventions such as the following:

- Reduction of the number of partners
- Consistent and correct use of condoms
- Male circumcision

2.3 Secondary Prevention
Secondary prevention involves activities to reduce STI complications of patients already infected including the following:

- Promotion treatment seeking
- Provision of quality care services to treat STIs
- Offer of support and counseling services
Chapter III. Diagnosis and Treatment

3.1 Syndromic Management
The syndrome approach is based on the identification and treatment of a set of symptoms and signs easily recognized based on the information and symptoms observed during the history and physical examination.

These syndromes, which may be caused by one or several STI germs, are the following:

1. Urethral discharge in men;
2. Vaginal discharge;
3. Genital ulceration;
4. Inguinal bubo;
5. Painful swelling of the scrotum;
6. Pelvic pain in women;
7. Venereal vegetation or growth (Condylomas);
8. Purulent conjunctivitis of the new born.

The syndrome approach enables one to carry out rapid presumptive diagnosis and to administer immediate treatment beginning with the first consultation. It enables the client to receive treatment without delay and increases the chances of healing. In all cases of STI infection warranting syndromic management, the following counselling and procedures should be provided:

- Tracing and treating the partner(s)
- Consistent and correct condom use
- Advice for local care when applicable
- HIV, HBV, HCV testing

Below is the summary of syndromic management of STIs and we recommend you refer to STIs Provider manual and specific algorithms (see on annexes different STI algorithms) for more detailed information on STIs management approach.
3.1.1 Syndromic Management for Urethral discharge

Figure 9: Algorithm of Urethral discharge diagnosis and treatment:

```
Receive/interview and examiner.
Press the urethra if necessary

Presence of discharge?
  Yes
  - Suspect gonococcus and Chlamydia
    - Ceftriaxone of 250 mg in one single dose AND
    - Azithromycine 1g in one single dose
    - Review patient in 7 days
  No

Persistence of syndromes despite good observance?
  No
  - Healing
  - Counselling
  Yes

Suspect trichomonas
  - Treat with first choice: Metronidazole of 2g or Tinidazole 2g in one single dose orally

Improvement
  No
  Refer
  Yes
  - Healing
  - Counselling
```

3.1.2 Syndromic Management for vaginal discharge

Figure 10: Algorithm of vaginal discharge diagnosis and treatment (Without speculum)

```
Vaginal Discharge
  Reception/Interview and examination
  Evaluate risk factors.

Risk is positive if:
- The partner has symptoms of urethritis.
- The patient presents at least the following
- Patient has two of the following:
  - Aged < 21 years;
  - Single;
  - Two or more sexual partners;

Suspect cervicitis (Gonococcus, Chlamydia, trichomonas + candida), treat with:
- Either Ceftriaxone of 250 mg in one single dose
- Azithromycine 1g in one single dose
- Metronidazole 2g or Tinidazole, 2g in a single dose in the evening.
- Clotrimazole 200 mg vaginal tablet in a single dose in the evening before going to bed for 3 days, or Fluconazole 150 mg in a single dose taken orally.

Suspect Vaginitis, (Bacterial vaginosis, trichomonas and Candida), treat with:
1st choice:
- Metronidazole 2g in one single dose in the evening during meals AND
- Clotrimazole 200 mg vaginal tablet in a single dose in the evening before going to bed for 3 days.
2nd choice:
- Tinidazole 2g in a single dose taken orally AND
- Fluconazole 150 mg in a single dose taken orally.

Refer if no improvement
```
Figure 11: Algorithm of vaginal discharge diagnosis and treatment (With speculum and bimanual examination)

3.1.3. Genital Ulceration
Genital ulceration is defined as any wound at the level of external genital organs of a man or a woman. It may be accompanied by inguinal lympho-adenopathy. Genital ulcerations represent 20 to 70% of the reasons for consultation of STI patients in Africa. These are in most cases the losses of tegument substance at the level of genital organs. They may be painful or painless, clean or dirty, fixed or mobile.
3.1.4 Inguinal bubo

The inguinal bubo is a tumefaction at the level of the groin or the inguinal ganglions. It is rarely the only manifestation of STIs and is generally associated with a genital ulceration. The most frequent symptoms are represented by pain associated with growth at the level of the groin but some buboes are not painful. On examination, pain or unilateral or bilateral inguinal fluctuations have been observed. The search of an STI associated usually leads to the one of the genital ulcerations (refer to the chapter on "genital ulceration") syndrome.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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.

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3.1.5 Painful swelling of the scrotum (PSS)

The painful swelling of the scrotum is a painful tumefaction of the scrotum where scrotal swelling is frequent. Symptoms may lead to sterility.

Figure 13: Algorithm of Inguinal Bubo diagnosis and treatment

Figure 14: Algorithm of Tumefaction of the scrotum diagnosis and treatment
3.1.6 Pelvic Pain in Women

Pelvic pain in women is defined as painful manifestations of the lower abdomen. Lower abdominal pain constitutes frequent reasons for consultations in emergency services. It is in most cases a manifestation of an evolving genital infection (cervicitis, endometritis, salpingitis, and ovaritis) that may be the cause of sterility and extra-uterine pregnancy.

Figure 15: Algorithm of Lower Abdominal Pain diagnosis and treatment

3.1.7. Venereal Vegetations

Venereal vegetations are cutano-mucous ex-growths on genital organs and/or in anal areas. The ex-growths due to STI include ano-genital condylomas or cumines condylomas and molluscum contagiosum. The condylomas may undergo malignant transformation with strong association to human papillomavirus. The presence of multiple extra genital lesions in an adult must suggest the possibility of the HIV infection.
Clinical aspects:

- **Ano-genital condylomas**
  - Genital warts may not cause any symptoms, or they may cause itching, burning, tenderness or pain. The ex-growth is over raised at the warty surface sitting on genital organs, around the anus or in the urethra.

- **Molluscum contagiosum**
  - The molluscum contagiosum is often asymptomatic but the diagnosis is generally not difficult.
  - Physical examination reveals small pimples of the skin colour, waxy, and umbilical at the centre. A brittle substance may rise by pressing these lesions.
  - **Differential diagnosis**

In ano-genital condyloma, it is necessary to eliminate the flat warts, which is suggestive of secondary syphilis, Molluscum contagiosum, inguinal granuloma, sebaceous cyst, tumours (benign or malignant) or normal purple pimples in the form of a pearl at the level of the crown of the glans.

The treatment of ano-genital condylomas consists in the destruction of the condylomatal by physical or clinical method (use of pomade or liquid podophilin, liquid nitrogen, silver nitrate crayon, surgery).

The treatment of molluscum contagiosum: silver nitrate crayon, curettage followed by the iodine dye.

In peripheral centres, the care and treatment of venereal vegetations hinges on:

- Education and counselling of the patient
- Promotion of HIV voluntary counselling and testing
- Referral
- Search for sexual partner(s).
3.1.8 Purulent Conjunctivitis of the new born

Purulent conjunctivitis of the new born baby (PCNB) is an ocular infection of the baby aged less than one month marked by red eyes with purulent and sticky secretions. PCNB is contracted at birth through contact with infectious vaginal secretions of the mother. It may lead to blindness, especially when it is due to *N. Gonorrhoea*. In the case of an infection due to Chlamydia, the new born may develop pneumonia and/or conjunctivitis.

The prophylaxis hinges on meticulous cleaning of the eyes, immediately after birth and the instillation of silver nitrate eye lotion at 1% or the application of the 1% tetracycline ointment.
Figure 17: Algorithm of conjunctivitis of the new born baby diagnosis and treatment

- Purulent secretions and/or blotch of the eye in the new born

Receive, interview and examine the child.

Presence of:
- Blotch of the yes;
- Bilateral or unilateral tumefaction of the eyelids;
- Purulent secretions?

Yes

- Treat the newborn, the mother and the partner for gonococci and chlamydia.

In the new born
- Ceftriaxone, 50 mg/Kg in an IM single dose (do not exceed the maximum dose of 125 mg).
- Azithromycin 20 mg/kg per day taken orally for 3 or Spectinomycin 25mg/kg IM single dose (not exceed max 75mg)
- Local care with physiological serum
  And treat the parents as per the algorithms above

No

- Reassure the mother.
- To advise the mother to return if necessary.

Continue treatment

Improveent?

Yes

No

Refer

3.2 Etiological Management
The aetiological approach uses laboratory tests with the support of data obtained from the interview and physical examination. It constitutes an ideal strategy in the care of STIs but it requires adequate laboratory and qualified personnel.
It is highly recommended at District, Provincial and Referral hospitals.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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. The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus. These guidelines would not have been finalized without the usual support of all the stakeholders who are involved in the domain of HIV-AIDS and other blood borne infections control in Rwanda.

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Dr Diane GASHUMBA
Minister of Health

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**Table 16: Clinical presentation and treatment in adults of common bacterial STIs**

<table>
<thead>
<tr>
<th>Clinical signs and symptoms</th>
<th>Diagnosis</th>
<th>Etiology</th>
<th>Diagnosis method/Lab</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Urethral discharge</td>
<td>Gonorrhea</td>
<td>Neisseria gonorrhoea</td>
<td>1. Gram Staining 2. Culture 3. NAT</td>
<td>- Ceftriaxone of 250 mg in one single dose or Cefixime 400mg oral single dose <strong>AND</strong> - Azithromycin 1g in one single dose</td>
</tr>
<tr>
<td>- Cervicitis and lower abdominal pain in women</td>
<td>Disseminated gonococcal infection</td>
<td>Neisseria gonorrhoea</td>
<td>1. Gram Staining 2. Culture 3. NAT</td>
<td>- Ceftriaxone of 1g IM/IV for every 24 hours for 24-48 hours or until clinical improvement and continue IM for total of 7 days <strong>AND</strong> - Azithromycin 1g in one single oral dose</td>
</tr>
<tr>
<td>- General symptoms: fever, polyarthritis, skin lesions - Usually no urogenital symptoms</td>
<td>Chlamydia trachomatis</td>
<td>Chlamydia trachomatis</td>
<td>1. Culture 2. ELISA 3. Direct Immunofluorescence 4. NAT</td>
<td>- Azithromycin 1 gr oral single dose <strong>OR</strong> - Doxycycline, 100 mg orally, twice daily for 14 days <strong>OR</strong> - Erythromycin, 500 mg orally, 4 times daily for 14 days</td>
</tr>
<tr>
<td>- Urethral discharge - Cervicitis and lower abdominal pain in women</td>
<td>Chlamydia trachomatis</td>
<td>Chlamydia trachomatis</td>
<td>1. Culture 2. ELISA 3. Direct Immunofluorescence 4. NAT</td>
<td>- Azithromycin oral single dose <strong>OR</strong> - Erythromycin, 500 mg orally, 4 times a day for 7 days <strong>OR</strong> - Amoxicillin, 500 mg orally, three times a day for 7 days</td>
</tr>
<tr>
<td>- Tender inguinal and/or femoral lymphadenopathy that is typically unilateral - Proctocolitis, including mucoid and/or hemorrhagic rectal discharges</td>
<td>Lymphogranuloma venereum</td>
<td>Chlamydia trachomatis</td>
<td>1. Culture 2. ELISA 3. Direct Immunofluorescence 4. NAT</td>
<td>- Azithromycin oral single dose <strong>OR</strong> - Doxycycline, 100 mg orally, twice daily for 21 days, <strong>OR</strong> - Erythromycin, 500 mg orally, 4 times daily for 21 days</td>
</tr>
<tr>
<td>- Painless ano-genital ulcers (chancr) - Inguinal tumefaction - Painless mucocutaneous lesions</td>
<td>Syphillis (primary, secondary, or latent syphillis of not more than two years’ duration)</td>
<td>Treponema pallidum</td>
<td>1. Screening: VDRL, RPR 2. Confirmation tests: Treponema tests: TPHA, FTA. Dark field microscopy, Direct fluorescent antibody test and NAT</td>
<td>- Benzathine benzylpenicillin 2.4 million IU IM, at a single session;</td>
</tr>
<tr>
<td>Cutaneous accidents (gums), cardio-vascular (aortitis) and neurological (neurosyphilis)</td>
<td>Late latent syphillis</td>
<td>Treponema pallidum</td>
<td>1. Screening: VDRL, RPR 2. Confirmation tests: Treponema tests: TPHA, FTA. Dark field microscopy, Direct fluorescent antibody test and NAT</td>
<td>- Benzathine benzylpenicillin, 2.4 million IU IM, once weekly for 3 consecutive weeks <strong>Alternative:</strong> procaine benzylpenicillin, 1.2 million IU IM, once daily for 20 consecutive days <strong>OR</strong> erythromycin, 500 mg orally, 4 times daily for 30 days</td>
</tr>
<tr>
<td>Genital ulcers with inguinal tumefaction (bubo) in most of the cases</td>
<td>Wet Chancre</td>
<td>Haemophilus ducreyi</td>
<td>1. Culture 2. NAAT</td>
<td>- Ciprofloxacin: 500 mg orally twice a day for 3 days <strong>OR</strong> Erythromycin base 500 mg orally three times a day for 7 days <strong>OR</strong> Ceftriaxone 250 mg intramuscularly (IM) in a single-dose <strong>OR</strong> Azithromycin 1 g orally in a single dose</td>
</tr>
<tr>
<td>Ulcerative vascular lesions on the genitals or perineum, subcutaneous granulomas (pseudobboes) - Hypertrophic, necrotic, or sclerotic variants - Extagenital infection can occur with extension of infection to the pelvis, intra-abdominal organs, bones, or the mouth.</td>
<td>Granuloma inguinale (Donovanosis)</td>
<td>Klebsiella granulomatis</td>
<td>Microscopy with dark-staining Donovan bodies on tissue crush preparation or biopsy</td>
<td>- Azithromycin orally 1gr Once per week or 500mg daily for at least3 weeks and until all lesions have completely healed <strong>OR</strong> - Ciprofloxacin 750 mg orally twice a day for at least 3 weeks and until all lesions have completely healed <strong>OR</strong> - Erythromycin base 500 mg orally four times a day for at least 3 weeks and until all lesions have completely healed</td>
</tr>
</tbody>
</table>
### Table 17: Clinical presentation and treatment of viral STIs in adults

<table>
<thead>
<tr>
<th>Clinical signs and symptoms</th>
<th>Diagnosis</th>
<th>Etiology</th>
<th>Diagnosis method/Lab</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Vesicular lesions and ano-genital ulcerations | Genital Herpes | Herpes virus of the simplex type 2 (HSV-2) | 1. Diagnosed clinically 2. Culture 3. NAAT | • Acyclovir 400 mg orally three times a day for 7–10 days OR  
Acyclovir 800 mg orally twice a day for 5 days  
**Alternative:**  
• Famciclovir 250 mg orally three times a day for 7–10 days OR  
Valacyclovir 1 g orally twice a day for 7–10 days |

| -Abnormal growth that is usually flat, papular, or pedunculated growths on the genital mucosa  
-Usually asymptomatic | Genital Warts | HPV 6 or 11 | Clinical diagnosis | • Topical treatment with Podofilox 0.5% solution or gel OR Podophyllin resin 10%–25% in a compound tincture of Benzoin OR  
• Cryotherapy with liquid nitrogen or cryoprobe, everyone 1-2 weeks until lesions disappears OR  
• Surgical removal |

| -Swollen ano-genital condylomes  
-Cervical condylomes | Genital Condylomes | Human papilloma Virus (HPV) | Clinical diagnosis | Destruction of the condylomatous tissue by physical and clinical method (Use of liquid nitrogen, silver nitrate crayon, curettage followed by the application of iodine dye). |
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Table 18: Clinical presentation and treatment of parasitic STIs in adults

<table>
<thead>
<tr>
<th>Clinical signs and symptoms</th>
<th>Diagnosis</th>
<th>Etiology</th>
<th>Diagnosis method/Lab</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse, malodorous, yellow-green vaginal discharge with vulvar irritation</td>
<td>Trichomoniasis</td>
<td><em>T. vaginalis</em></td>
<td>Direct wet-mount microscopy OR NAT (Test of choice)</td>
<td>• Metronidazole 2 g orally in a single dose OR Tinidazole 2 g orally in a single dose</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Pediculosis Pubis</td>
<td>Pubic lice</td>
<td>Clinical diagnosis</td>
<td>• Personal hygiene</td>
</tr>
<tr>
<td>Cutaneous rash, itching</td>
<td>Scabies</td>
<td><em>Sarcoptes scabiei</em></td>
<td>Clinical diagnosis</td>
<td>• Permethrin 5% cream one application per day OR Lindane 1% OR Benzocaine de Benzyll</td>
</tr>
</tbody>
</table>

Table 19: Clinical presentation and treatment of yeast STIs in adults

<table>
<thead>
<tr>
<th>Clinical signs and symptoms</th>
<th>Diagnosis</th>
<th>Etiology</th>
<th>Diagnosis method/Lab</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus, vaginal soreness, dyspareunia, external dysuria, and abnormal vaginal discharge</td>
<td>Vulvovaginal Candidiasis</td>
<td>Usually caused by <em>C. albicans</em>, but occasionally by other <em>Candida</em> species</td>
<td>Wet preparation or Gram stain of vaginal discharge culture</td>
<td>• Polycynax vaginal pill OD for 12 days OR • Fluconazole 150mg single oral dose • Clotrimazole 2% cream 5 g intravaginally for 3 days OR • Miconazole 200 mg vaginal suppository, one for 3 days</td>
</tr>
</tbody>
</table>
### 3.3 STI Management in Special Cases

#### 3.3.1 Treatment of STIs in children and adolescents

**Table 20: STIs in children and adolescents according to syndrome**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Organisms/Diagnoses</th>
<th>Treatment of adolescent&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Treatment of infant/child</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urethritis and cervicitis</strong></td>
<td><em>Neisseria gonorrhoeae,</em> <em>Chlamydia trachomatis,</em> <em>Mycoplasma genitalium,</em> possibly <em>Ureaplasma urealyticum,</em> and sometimes <em>Trichomonas vaginalis</em> and Herpes simplex virus (HSV)</td>
<td>• <em>Ceftriaxone,</em> 250 mg, IM, in a single dose&lt;sup&gt;b&lt;/sup&gt; <strong>OR</strong> <em>Cefixime,</em> 400 mg, orally, in a single dose&lt;sup&gt;b&lt;/sup&gt; <strong>AND</strong> Azithromycin, 1 g, orally, in a single dose <strong>OR</strong> Doxycycline, 100 mg, orally, twice a day for 7 days</td>
<td><strong>Children &lt;45 kg:</strong> <em>Ceftriaxone,</em> 125 mg, IM, in a single dose <strong>OR</strong> <em>Cefixime,</em> 8 mg/kg (maximum 400 mg, orally, in a single dose) <strong>AND</strong> Azithromycin, 1 g, orally, in a single dose <strong>OR</strong> Doxycycline, 100 mg, orally, twice a day for 7 days <strong>Children ≤45 kg and &lt;8 y of age:</strong> Erythromycin base or Ethylsuccinate, 50 mg/kg per day, orally, in 4 divided doses (maximum 2 g/day) for 14 days <strong>Children ≥45 kg but &lt;8 y of age:</strong> Azithromycin, 1 g, orally, in a single dose <strong>Children ≥45 kg and ≥8 y of age:</strong> Azithromycin, 1 g, orally, in a single dose <strong>OR</strong> Doxycycline, 100 mg, orally, twice a day for 7 days</td>
</tr>
<tr>
<td><strong>Prepubertal vaginitis (STI related):</strong></td>
<td><em>N gonorrhoeae</em>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>See adult treatment</td>
<td><strong>Children &lt;45 kg:</strong> <em>Ceftriaxone,</em> 125 mg, IM, in a single dose</td>
</tr>
<tr>
<td></td>
<td><em>C trachomatis</em>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>See adult treatment</td>
<td><strong>Children &lt;45 kg and &lt;8 y of age:</strong> Erythromycin base or Ethylsuccinate, 50 mg/kg per day, orally, in 4 days</td>
</tr>
</tbody>
</table>

<sup>a</sup> STIs in children and adolescents according to syndrome
### Table: Treatment of Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Organisms/Diagnoses</th>
<th>Treatment of adolescent&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Treatment of infant/child</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>divided doses (maximum 2 g/day) for 14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Children ≥45 kg but &lt;8 y of age:</strong> Azithromycin, 1 g, orally, in a single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Children ≥45 kg and ≥8 y of age:</strong> Azithromycin, 1 g, orally, in a single dose</td>
<td>OR Doxycycline, 100 mg, orally, twice a day for 7 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Children &lt;45 kg:</strong> Metronidazole, 15 mg/kg per day, orally, in 3 divided doses (maximum 2 g/day) for 7 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Children &lt;45 kg:</strong> Metronidazole, 15 mg/kg per day, orally, in 2 divided doses (maximum 1 g/day) for 7 days</td>
<td></td>
</tr>
<tr>
<td>T vaginalis</td>
<td>See adult treatment</td>
<td><strong>Children &lt;45 kg:</strong> Metronidazole, 15 mg/kg per day, orally, in 3 divided doses (maximum 2 g/day) for 7 days</td>
<td></td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>See adult treatment</td>
<td><strong>Children &lt;45 kg:</strong> Metronidazole, 15 mg/kg per day, orally, in 2 divided doses (maximum 1 g/day) for 7 days</td>
<td></td>
</tr>
<tr>
<td>HSV—primary infection</td>
<td>Acyclovir, 400 mg, orally, 3 times/day for 7–10 days OR Acyclovir, 200 mg, orally, 5 times/day for 7–10 days OR Famciclovir (250 mg, orally, 3 times/day) for 7–10 days OR Valacyclovir (1 g, orally, twice daily) for 7–10 days</td>
<td><strong>Children &lt;45 kg:</strong> Acyclovir, 80 mg/kg per day, orally, in 3–4 divided doses (maximum 1.2 g/day) for 7–10 days OR Valacyclovir, 40 mg/kg per day, orally, in 2 divided doses for 7–10 days</td>
<td></td>
</tr>
<tr>
<td>Adolescent vulvovaginitis</td>
<td>Metronidazole, 2 g, orally, in a single dose OR Tinidazole, 2 g, orally, in a single dose</td>
<td><strong>Children &lt;45 kg:</strong> Metronidazole, 500 mg, orally, twice daily for 7 days OR Metronidazole gel 0.75%, 1 full applicator (5 g), intravaginally, once a day for 5 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>TV</strong> vaginalis</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td></td>
<td>Bacterial vaginosis</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Syndrome</td>
<td>Organisms/Diagnoses</td>
<td>Treatment of adolescent&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Treatment of infant/child</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR Clindamycin cream 2%, 1 full applicator (5 g), intravaginally at bedtime, for 7 days</td>
<td></td>
</tr>
<tr>
<td>Candida species</td>
<td>See Table 4.4, Recommended Regimens for Vulvovaginal Candidiasis</td>
<td>…</td>
<td></td>
</tr>
<tr>
<td>HSV—primary infection</td>
<td>Acyclovir, 400 mg, orally, 3 times/day for 7–10 days</td>
<td>…</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR Famcyclovir, 250 mg, orally, 3 times/day for 7–10 days</td>
<td>…</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR Valacyclovir, 1 g, orally twice/day for 7–10 days</td>
<td>…</td>
<td></td>
</tr>
<tr>
<td>Pelvic inflammatory disease (PID)</td>
<td>&lt;i&gt;N. gonorrhoeae&lt;/i&gt;, &lt;i&gt;C. trachomatis&lt;/i&gt;, anaerobes, coliform bacteria, and &lt;i&gt;S. species&lt;/i&gt;</td>
<td>- See adult treatment</td>
<td>PID occurs rarely, if at all, in pre-pubertal girls</td>
</tr>
<tr>
<td>Syphilis</td>
<td>&lt;i&gt;T. pallidum&lt;/i&gt;</td>
<td>See <a href="#">Syphilis</a></td>
<td><a href="#">Children &lt;45 kg:</a> Same as for congenital syphilis</td>
</tr>
<tr>
<td>Genital ulcer disease</td>
<td>&lt;i&gt;T. pallidum&lt;/i&gt;</td>
<td>Same as for syphilis</td>
<td><a href="#">Children &lt;45 kg:</a> Same as for congenital syphilis</td>
</tr>
<tr>
<td>HSV—primary infection</td>
<td>See prepubertal vaginitis</td>
<td>…</td>
<td><a href="#">Children &lt;45 kg:</a> See pre-pubertal vaginitis</td>
</tr>
<tr>
<td>&lt;i&gt;Haemophilus ducreyi&lt;/i&gt; (chancre)</td>
<td></td>
<td>Azithromycin, 1 g, orally, in a single dose</td>
<td><a href="#">Children &lt;45 kg:</a> Ceftriaxone, 50 mg/kg, IM, in a single dose (maximum 250 mg) OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR Ceftriaxone, 250 mg, IM, in a single dose</td>
<td><a href="#">Children &lt;45 kg:</a> Ceftriaxone, 50 mg/kg, IM, in a single dose (maximum 250 mg) OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR Ciprofloxacin, 500 mg, orally, twice daily for 3 days&lt;sup&gt;c&lt;/sup&gt;</td>
<td><a href="#">Children &lt;45 kg:</a> Azithromycin, 20 mg/kg, orally, in a single dose (maximum 1 g)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR Erythromycin base, 500 mg, orally, 3 times/day for 7 days</td>
<td></td>
</tr>
<tr>
<td>&lt;i&gt;Klebsiella granulomatis&lt;/i&gt;</td>
<td>Doxycycline, 100 mg, orally, twice a day for at least 3 wk and until all lesions have healed</td>
<td>…</td>
<td></td>
</tr>
</tbody>
</table>
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**Syndrome** | **Organisms/Diagnoses** | **Treatment of adolescent** | **Treatment of infant/child**
---|---|---|---
Sexually acquired epididymitis | *(granuloma inguinale [Donovanosis]) d* | completely OR Azithromycin, 1 g, orally, once/wk for at least 3 wk and until all lesions have healed completely OR Ciprofloxacin, 750 mg, orally, twice a day for at least 3 wk and until all lesions have healed completely OR Erythromycin base, 500 mg, orally, 4 times/day for at least 3 wk and until all lesions have healed completely OR Trimethoprim-sulfamethoxazole, 1 double-strength (160 g/800 mg) tablet, orally, twice a day for at least 3 wk and until all lesions have healed completely | ...

Sexually acquired epididymitis | *C trachomatis, N gonorrhoeae* | Ceftriaxone, 250 mg, IM, in a single dose PLUS Doxycycline, 100 mg, orally, twice daily for 10 days | ...

Enteric organisms (for patients allergic to cephalosporins and/or tetracycline) | Levofloxacin, 500 mg, orally, once daily for 10 days OR Ofloxacin, 300 mg, orally, twice a day for 10 days | ...

Gonococcal infections of the pharynx | *N gonorrhoeae* | Ceftriaxone, 250 mg, IM, in a single dose Or Cefixime oral 400mg single dose AND Azithromycin 1 gr oral single dose | Ceftriaxone, 125 mg, IM, in a single dose

Anogenital warts | Human papillomavirus | Patient-applied: Podofilox 0.5% solution or gel OR Imiquimod 5% cream OR Sinecatechins 15% ointment | Children <45 kg: Same as for adolescents

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*For children under 45 kg, follow the treatment guidelines for adolescents.*
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___________________________
Dr Diane GASHUMBA
Minister of Health

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Organisms/Diagnoses</th>
<th>Treatment of adolescent(^a)</th>
<th>Treatment of infant/child</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cryotherapy OR Podophyllin resin 10%–25(^c) OR Trichloroacetic acid OR Bichloroacetic acid OR Surgical removal</td>
<td></td>
</tr>
</tbody>
</table>

IM indicates intramuscularly; STI, sexually transmitted infection. For laboratory diagnosis refer to adult table.
### 3.3.2 Treatment of STIs in Neonates

**Table 21: Treatment of STIs in Neonates**

<table>
<thead>
<tr>
<th>Presence of Congenital STI</th>
<th>Pathogen</th>
<th>Clinical Manifestations and Treatment</th>
</tr>
</thead>
</table>
| - Inflammation of the conjunctiva and mucopurulent discharge from the eye | Neisseria gonorrhoea | 1. Gram Staining  
2. Culture  
3. NAT  
- Ceftriaxone of 25-50 mg/kg IM or IV in one single dose not exceeding 125 mg  
- Azithromycin 1 g in one single dose  
- Ceftriaxone 50 mg/kg in an IM single dose (do not exceed the maximum dose of 125 mg) AND  
- Azithromycin 20 mg/kg per day taken orally for 3 days OR  
Spectinomycin 25 mg/kg IM single dose (not exceed max 75 mg)  
- Local care with physiological serum |
| Mostly asymptomatic | Neisseria gonorrhoea | 1. Gram Staining  
2. Culture  
3. NAT  
- Ceftriaxone of 25-50 mg/kg IM or IV in one single dose not exceeding 125 mg  
- Azithromycin 1 g in one single dose  
- Ceftriaxone 50 mg/kg in an IM single dose (do not exceed the maximum dose of 125 mg) AND  
- Azithromycin 20 mg/kg per day taken orally for 3 days OR  
Spectinomycin 25 mg/kg IM single dose (not exceed max 75 mg)  
- Local care with physiological serum |
| Inflammation of the conjunctiva and mucopurulent discharge from the eye | Neisseria gonorrhoea | 1. Culture  
2. ELISA  
3. Direct Immunofluorescence  
4. NAT  
- Erythromycin syrup, 50 mg/kg per day orally, in 4 divided doses for 14 days |
| Cutaneous, bony, and vascular accidents | Treponema pallidum | 1. Screening: VDRL, RPR  
2. Confirmation tests:  
Treponemal tests: TPHA, FTA. Dark field microscopy, Direct fluorescent antibody test and NAT  
- Aqueous benzylpenicillin 100 000–150 000 IU/kg/day administered as 50 000 IU/kg/dose IV every 12 hours, during the first 7 days of life and every 8 hours thereafter for a total of 10 days  
- Aqueous benzylpenicillin, 200 000–300 000 IU/kg/day IV OR IM, administered as 50 000 IU/kg/dose every 4–6 hours for 10–14 days  
Alternative:  
Erythromycin, 7.5–12.5 mg/kg orally, 4 times daily for 30 days(TBD By Paediatricians) |
| - Ocular, dental, vascular, additive, bone and neurological accidents -These manifestations may lead to death or functional loss (blindness). | Treponema pallidum | 1. Screening: VDRL, RPR  
2. Confirmation tests:  
Treponemal tests: TPHA, FTA. Dark field microscopy, Direct fluorescent antibody test and NAT  
- Aqueous benzylpenicillin 100 000–150 000 IU/kg/day administered as 50 000 IU/kg/dose IV every 12 hours, during the first 7 days of life and every 8 hours thereafter for a total of 10 days  
- Aqueous benzylpenicillin, 200 000–300 000 IU/kg/day IV OR IM, administered as 50 000 IU/kg/dose every 4–6 hours for 10–14 days  
Alternative:  
Erythromycin, 7.5–12.5 mg/kg orally, 4 times daily for 30 days(TBD By Paediatricians) |
| Maternal virologic testing or presumed by observation of maternal lesions | Neonatal Herpes | 1. Diagnosed clinically  
2. Antibody detection of HSV-2  
3. Culture  
4. NAAT  
- Acyclovir 20 mg/kg IV every 8 hours for 21 days for disseminated and CNS disease OR for 14 days for disease limited to the skin and mucous membranes. |
Purulent conjunctivitis of the new born (less than 1 month of age)

- Red eyes with purulent and sticky secretions.
- Contracted at birth through contact with infectious vaginal secretions of the mother.
- May lead to blindness, especially when due to *N. Gonorrhoea*. In the case of *Chlamydia*, the new born may also develop pneumonia.
- Prophylaxis: meticulous cleaning of eyes immediately after birth and application of silver nitrate eye 1% lotion or tetracycline 1% ointment.

**Table 22: Purulent conjunctivitis of the new born**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Clinical</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>N. gonorrhoea</em></td>
<td>Conjunctivitis: red eyes with sticky, purulent discharge, pruritus</td>
<td>Gram – diplococcic, “coffee bean” can be seen in secretions</td>
<td>Ceftriaxone 50mg/kg single dose IM (maximum 125mg)</td>
</tr>
<tr>
<td><em>C. trachomatis</em></td>
<td>Conjunctivitis and pneumonia</td>
<td>Serology can be positive in a baby with severe chlamydial disease</td>
<td>Erythromycin 50mg/kg/day in 4 doses X 14 days</td>
</tr>
</tbody>
</table>

3.3.3 Cases of sexual abuse and aggression against children and adolescents

Sexual abuse occurs when a child or adolescent engages in sexual activities that he or she may not understand for which he or she is not prepared for. The child or adolescent cannot therefore give consent and these activities violate the law. These sexual activities include any forms of sexual contact such as sexual relations (including oral, genital, ano-genital, genito-genital) and fondling.

3.3.3.1 Clinical signs of sexual abuse

Clinical signs of sexual abuse include: genital discharges, tear or the absence hymen, fissure or anal gaping, trauma of the perinea, recto virginal fistula or vesico-vaginal fistulae, pelvic pain. There can also be signs linked to physical trauma and behavioural disorders. (See Table 25)
### Table 23: Clinical signs of sexual abuse in children

<table>
<thead>
<tr>
<th>Signs</th>
<th>Girls</th>
<th>Boys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genitals</td>
<td>Absence or tear of the hymen; Fissure or anal openness; Trauma of the perineum; Vesico-vaginal fistula; Recto vaginal fistula; Pelvic pain; Presence of STI.</td>
<td>Anal gaping, anal fissure, recto anal fistula Presence of STI.</td>
</tr>
<tr>
<td>Other signs</td>
<td>Cutaneous trauma; Marked docility on examination; Exaggerated fear by the patient of a parent or close relative.</td>
<td></td>
</tr>
</tbody>
</table>

#### 3.3.3.2. Clinical examination

Initial clinical examination should include the following:

- To collect data and information on the circumstances in which the sexual abuse occurred;
- To determine if possible, the time separating the aggression and the date of consultation;
- To carry out meticulous physical examination in search of the signs of STIs (genital discharges, ulcerations and genital vesicles, condyloma);
- To collect anal samples in the two sexes, vaginal swab in case of a young girl, and urethral samples in case of a boy in the view to search for gonococcus, chlamydia, Trichomonas vaginalis;
- To carry out serological tests for HIV, hepatitis B and syphilis;
- To carry out the pregnancy test in case of a young girl who has already started having menstruations.
- To search for clinical signs of STIs and carry out serological tests for HIV, hepatitis B and syphilis of the aggressor or the suspected perpetrator of the aggression if he/she has been identified.

A follow-up examination should be done at 3 months to repeat the serological tests for HIV, hepatitis B and syphilis in the child (especially if the initial tests were negative.
3.3.3.3 Treatment

- If the pregnancy test is negative, prescribe within 72 hours (following the aggression or sexual abuse) urgent contraception;
- If HIV serology is positive in the aggressor, treat the child and start the ARV treatment. The results are the best when treatment is started within 6 hours that follow the aggression quite before 24 hours and do not exceed 72 hours;
- If a germ is isolated, it is necessary to treat the child by taking into account its sensitivity to antibiotics (or treatment according to the STI syndrome identified);
- If no germ is isolated and if there exist other risk factors that have been identified in the aggressor or if the aggressor presents STI or has recent precedents of STIs, in this case there is need to provide presumptive treatment. This treatment must take into account the syndrome of the suspected STI in the aggressor.
- In all cases, the child should be monitored for psychological issues that may arise
- In case the HIV serology is positive, monitoring and treatment of the child must respect the recommendations for the medical care of HIV.
3.3.4 Care and treatment of STIs in sex workers

Sex workers are vulnerable groups and core groups for the transmission of HIV and other STIs. Given the high prevalence of HIV and other STIs in female sex women, active diagnosis of STIs is highly recommended. In practice, during the first visit, every female sex worker should be systematically treated for PID and presumptive gonococcus, chlamydia and trichomonas. Treatment should include:

- Ceftriaxone of 250 mg IM or Cefixime 400mg in one single dose
- Azithromycine 1g in one single dose
- Metronidazole, 2g in a single dose in the evening during meals or Tinidazole, 2g in a single dose orally.

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**Figure 18: Algorithm of Care and treatment of STI in sex abuse in children.**
For subsequent visits, treatment will be given according to the present syndromes. During all visits, counselling activities usually done in general populations should also be done for sex workers. These activities include promoting and providing condoms, treating permanent partners, proposing HIV testing and promoting the participation in health promotion activities.

### 3.3.5 Care and treatment of STIs in men who have sex with men (MSM)

Subgroups of MSM are at high risk for HIV infection and other viral and bacterial STIs. MSM, including those with HIV infection, should routinely undergo non-judgmental HIV and other STIs risk assessment and client-centered prevention counseling to reduce the likelihood of acquiring or transmitting HIV or other STIs. Health providers should be informed about the local community resources available to assist MSM. Clinicians also should routinely ask MSM about symptoms consistent with common STIDs, including urethral discharge, dysuria, genital and perianal ulcers, regional lymphadenopathy, skin rash, and anorectal symptoms consistent with proctitis, including discharge and pain on defecation or during anal intercourse. Care providers should perform appropriate diagnostic testing on all symptomatic patients.

Routine laboratory screening for common STIs (HIV serology, syphilis serology, a test for urethral infection with N. gonorrhoeae and C. trachomatis in men who have had insertive intercourse, a test for rectal infection with N. gonorrhoeae and C. trachomatis in men who have had receptive anal intercourse, a test for pharyngeal infection§ with N. gonorrhoeae in men who have had receptive oral intercourse) is indicated for all sexually active MSM because of the high prevalence of asymptomatic STIs in MSM. Multisite (pharyngeal, urethral, anal) screening is advisable.

### 3.3.6 Persons in Correctional Facilities

Screening for symptomatic and asymptomatic of STIs in detention facilities and jails facilitates the identification and treatment of persons with infections. This will eliminate complications for the individual and will reduce the prevalence of STIs among detainees who are released back into the local community.

### 3.3.7 Care of sexual partners

The care of sexual partners, even in the absence of any sign constitutes an important component for the control of STIs and hence the HIV infection. It enables the breaking of the chain of transmission through:
Prevention of the infection of the “case index”;
Prevention of secondary infections from infected partner(s) of the “case index”;
It especially based on the approach of the notification of partners to have them treated and counselled.
In a health facility where the etiologic approach is possible, asymptomatic sexual partners should be tested before initiating STI treatment.

3.4 Complications
Late, untreated or poorly treated STIs may lead to the following complications in women, men and newborns

3.4.1 Complications in men
The following complications can be observed:
- Orchi-epididymitis;
- Prostatitis;
- Sterility;
- Urethral constriction;

In the absence of treatment, 10 to 30% of patients suffering from gonococcus urethritis develop an epididymitis that may make 20 to 40% of client’s sterile. In developing countries, one man out of seven suffering from gonococcus develops urethral constriction.

3.4.2 Complications in women
The most frequent complications are the following:
- Pelvic inflammatory disease (PID) or pelvic inflammatory syndrome (PIS);
- Sterility;
- Extra-uterine pregnancy;
- Cervical cancer;
- Complication during pregnancy: abortion, still birth, underweight new-born following premature childbirth or delay in delivery.

3.4.3 Complications in newborns
Due to vertical transmission, the following may be observed:
- Neonatal conjunctivitis due to Neisseria gonorrhoea and/or due to Chlamydia trachomatis that may lead to blindness;
- A pulmonary infection due to Chlamydia trachomatis;
- Congenital syphilis due to Treponema pallidum;
- Premature childbirth,
- Underweight
3.4.4 Consequences due to complications

Consequences linked to STIs are economic, social or health aspects with direct repercussions on the individual himself/herself, the family, the community and even the state.

Economic consequences include both direct and indirect costs. Direct costs incurred include increase in out-of-pocket spending for individuals and increase in budget spending for governments. Indirect costs incurred include decline in productivity through sick leave, inability to work, deaths and social consequences such as marital conflicts.

Chapter IV. Programmatic Implementation

- Provide friendly STIs care and treatment to avoid stigmatization;
- Contact tracing and screening of STIs patients
- Advocate for a better diagnosis and management

Complete care of STIs includes:

1) IEC/BCC (focus on risk factors, STIs and HIV relationship)
2) Systematic screening of syphilis in pregnant women
3) Systematic screening of STIs for new-born, adolescents and adults
4) Screening and systematic treatment of FSW and MSM
5) Carry out the correct diagnosis;
6) Provide correct antimicrobial treatment corresponding to the syndrome of STI, corresponding to the clinical diagnostic of STI or corresponding to the micro-organism of the STI;
7) Explain the adherence of the treatment;
8) Demonstrate the correct condom use and to make them available and accessible;
9) Provide counselling on the treatment of partners and to give the patient an orientation form for the sexual partner so that he/she can send it to his/her partner(s); 10) Systematic HTC.
The current HBV, HCV and STIs National Guidelines 2018 for prevention and management of hepatitis B, hepatitis C and STIs were developed in line with World Health Organization guidelines published in 2017. It thus responds to the Ministry of Health 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.

The dissemination of the current guidelines will improve skills of health care providers and the quality of life of people infected of the mentioned virus.

These guidelines would not have been finalized without the usual 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 hepatitis technical working group and respective organizations that contributed to the development of this document.

References


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Dr Diane GASHUMBA
Minister of Health