SECTION 14

VIRAL HEPATITIS

This section provides information about viral hepatitis for people living with HIV.

What is the liver? What is viral hepatitis? What is hepatitis B virus (HBV)? How is HBV transmitted? How can you prevent HBV? What happens to someone with HBV? What are the symptoms? What tests and treatments do people with HBV need?

What is hepatitis C virus (HCV)? How is HCV transmitted? How can you prevent HCV? What happens to someone with HCV? What are the symptoms? What tests and treatments do people with HCV need?

After reading this section, you will have a basic understanding of:

- What the liver is
- What hepatitis is
- What HBV and HCV are
- HIV and viral hepatitis
- How someone can get HBV
- How to prevent HBV
- What can happen to someone with HBV
  - HBV symptoms
- HBV testing
- HBV treatment
- How someone can get HCV
- How to prevent HCV
- What can happen to someone with HCV
  - HCV symptoms
- HCV testing
- HCV treatment
- Viral hepatitis Q and A

WHAT IS THE LIVER?

The liver is the largest organ inside inside of the body. It sits over the stomach, on the right side of the body. Everything someone eats and drinks, all the medicines they take, including antiretrovirals (ARV), and even the air they breathe passes through the liver.

The liver filters out toxins and bacteria from the bloodstream, and works as the body's processing plant, turning sugar into energy, storing iron, making cholesterol, and helping to distribute fat through the body. The liver also makes proteins that help blood to clot, and immune factors to resist infections.

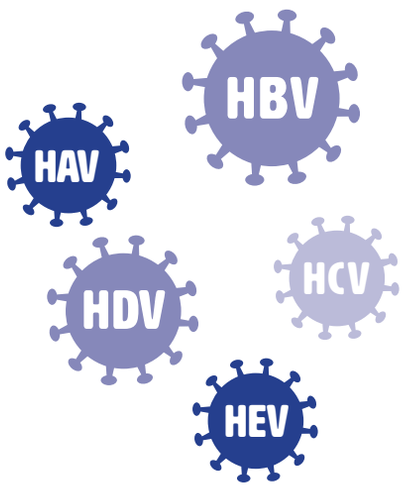
The liver is the only internal organ that can heal and grow back to its full size if it is cut during surgery or from an injury. But once the liver has become badly scarred from viral hepatitis, it stops being able to heal itself. A person cannot survive without a liver.

WHAT IS HEPATITIS?

Hepatitis means swollen liver. Many things can cause liver swelling, such as inhaling toxic fumes, taking certain medicines, drinking large amounts of alcohol and bacterial infections.

WHAT IS VIRAL HEPATITIS?

Hepatitis can be caused by viruses – hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV). These viruses were named with a letter of the alphabet, in the order that they were discovered.



HIV AND VIRAL HEPATITIS

HIV and viral hepatitis are transmitted in some of the same ways, making co-infection with HBV and/or HCV common among people living with HIV.

HIV itself can cause liver damage, even in people who do not have viral hepatitis. HIV increases the risk and rate of liver damage among people with viral hepatitis. Treating HBV and curing HCV among people living with HIV lowers these risks.

HBV can be treated, and researchers are working on different strategies to cure it. Currently, as with HIV, treatment for HBV is lifelong. TDF works as a treatment for both HIV and HBV. For this reason, people who are HIV/HBV co-infected should be taking antiretroviral treatment (ART) that includes TDF.

If people living with HIV/HBV co-infection switch their ARVs, they need to continue TDF and lamivudine (3TC) or emtricitabine (FTC) for their HBV.

HCV can usually be cured by 12 weeks of once-daily, oral direct-acting antiviral (DAA) treatment. Most DAAs can be used with ARVs, but some people may need to switch their ARVs during HCV treatment to avoid drug interactions. DAAs are just as likely to work for people who are living with HIV and HCV as people who have HCV alone.

VIRAL HEPATITIS AND ARVS

Antiretroviral treatment (ART) is recommended for everyone who is living with HIV, including people who are co-infected with viral hepatitis. Although people living with HIV and HBV and/or HCV are at higher risk for liver toxicity from some ARVs (darunavir/ritonavir, dolutegravir, efavirenz, lopinavir/ritonavir, nevirapine, raltegravir and tenofovir [TDF]), the benefits of HIV treatment outweigh the risk of liver toxicity.

HEPATITIS B VIRUS (HBV)

Hepatitis B is a virus that can cause serious, life-threatening liver damage. South Africa is home to one of world's largest burdens of HBV.

An estimated 6.7 percent of South Africans — or 3.4 million people — are living with HBV; 5-23% of the country's 7.7 million people living with HIV are co-infected with HBV. The highest rate of HBV is found among people living with HIV ages 25-30 years.

HOW DO YOU GET HBV?

HBV is 100 times more infectious than HIV, It is transmitted by body fluids (blood, semen, vaginal fluid and saliva).

People can get HBV through:

- Vertical transmission (from a mother with HBV to her baby) during pregnancy, at delivery and up to 28 days after birth
- Condomless anal, vaginal, or oral sex with a person who has HBV
- Sharing equipment to inject drugs that has been used by someone with HBV
- Receiving an organ transplant or transfusion with unscreened blood or blood products, especially before 1992
- Medical or dental care with shared, unsterilised equipment that was used on someone with HBV
- Sharing tattooing needles, ink and inkwells with someone who has HBV
- Traditional scarification practices
- Female genital mutilation
- Needlestick accidents and other occupational exposures to blood from a person with HBV
- Sharing personal care items that may have blood on them, such as razors, toothbrushes and manicuring implements.

HEPATITIS D VIRUS (HDV)

People who already have HBV can get another hepatitis virus, called HDV, which is passed from person to person the same way as HBV.

HDV increases the risk and speeds up the rate of liver damage among people living with HBV. HDV can be treated with pegylated interferon, but it is expensive, has serious side effects and is not very effective; more research on HDV treatment is needed.

HOW TO PREVENT HBV

HBV can be prevented in some of the same ways as HIV: by using condoms for anal, vaginal and oral sex, never sharing needles, syringes and other injection equipment – and by getting vaccinated. The vaccine will prevent HBV and HDV, since people cannot get HDV unless they already have HBV.

Table 1. HBV Vaccination Schedule

	First Dose	Second Dose	Third Dose	Booster
Infants	Provide first vaccine dose within 24 hours of birth	At least 1 month after the first dose	At least 1 month after the second dose	
Children	Provide first vaccine dose on day 0	At least 1 month after the first dose	1-12 months weeks after the second dose	
Adults	Provide first vaccine dose on day 0	At least 1 month after the first dose	At 1-12 months weeks after the second dose	
People living with hiv who did not respond to their first hbv vaccine doses	Re-vaccinate; doubling the dose or giving additional doses may increase the response, but limited evidence exists to support these schedules.			
People who inject drugs	Offer rapid or very rapid vaccine regimen; provide first vaccine dose on day 0	**Rapid:** 1 month after first dose	**Rapid:** 1 month after second dose	Rapid and very rapid: 12 months after the first dose
		Very rapid: 7 days after the first dose	**Very rapid:** 21 days after the first dose	

Sources: South Africa. National Guidelines for the Management of Viral Hepatitis. December 2019; in press. World Health Organization. Hepatitis B Vaccine. Undated. https://www.who.int/ith/vaccines/hepatitisB/en/

Currently, South Africa does not require maternal hepatitis B surface antigen (HBsAG) screening or HBV birth-dose vaccination, nor it does not have a "catch-up" immunisation programme for people who were not vaccinated, missed a vaccine dose or did not complete a vaccine series.

For people who have not been vaccinated, or did not respond to vaccination, HBV post-exposure prophylaxis (PEP) with hepatitis B immunoglobulin (HBIG) and HBV vaccination are effective.

South African guidelines recommend PEP for:

- Babies born to mothers with HBV, especially when given within 12 hours of birth
- Occupational exposures (needlestick injuries or exposure to blood or body fluids) from someone known or likely to have HBV
- Sex or needle-sharing partners of someone known to have HBV, or of unknown HBV status
- People who have been sexually assaulted by someone known to have HBV, or of unknown HBV status.

WHAT HAPPENS TO PEOPLE WITH HBV?

A person can only get HBV once — and they can only get HDV if they already have HBV, or if they get both viruses at the same time.

HBV can become a lifelong infection. Chronic HBV is most likely in people infected at birth (75-90%) or when they were under age six years (25-50%) and people living with HIV (30-90%). If HBV does not go away within six months, it is considered to be a chronic infection.

Untreated HBV causes serious liver scarring (called cirrhosis), liver failure and liver cancer in 20-30% of people. The risk for liver damage from HBV is higher among:

- People living with HIV, who are more likely to develop cirrhosis and/or liver cancer, especially if they have a low CD4 cell count (less than 200 cells/mm3)
- People who also have HCV and/or HDV
- Older people
- People who have had HBV for many years
- People with a family history of liver cancer
- People of Asian or African ancestry
- People who have been exposed to aflatoxins (poisonous substances made by certain kinds of mold that are found worldwide and can contaminate food crops)
- Heavy drinkers — over 3 drinks of any kind (beer, wine or spirits) a day for women and over 4 drinks per day for men
- Cigarette smokers
- Men

HBV SYMPTOMS

Children usually do not feel ill from HBV. The most common symptoms of a recent HBV infection among adolescents and adults are:

- Nausea
- Vomiting
- Stomach pain
- Appetite and weight loss
- Weakness and tiredness
- Fever, muscle or joint pain
- Yellowing skin and eyes (jaundice)
- Dark urine

There is no treatment for acute HBV, but symptoms will go away on their own. Many people with chronic HBV have no symptoms until serious liver damage has developed.

HBV TESTING

HBV can be diagnosed with blood tests.

In South Africa, HBsAg testing is used to diagnose HBV infection, although healthcare workers may do additional tests, which can tell someone if:

- They have not been infected with HBV, and should be vaccinated
- They have been vaccinated, and are protected against HBV
- They had HBV in the past, and the infection is resolved
- They were recently infected with HBV
- They are recovering from HBV
- They have chronic HBV.

HBV TREATMENT

The goal of current HBV treatment is to prevent complications such as cirrhosis, liver failure and liver cancer. As with HIV treatment, HBV treatment is currently lifelong, although researchers are looking at ways to cure HBV.

In South Africa, ART is recommended for all people living with HIV – regardless of CD4 count – including people living with HIV/HBV coinfection. HIV and HBV can be treated with the same drugs, since some ARVs work against both viruses.

People who are living with HIV/HBV should be treated with a combination that includes ARVs that work against both viruses; these are TDF with FTC) or 3TC.

If someone who is living with HIV/HBV co-infection switches their ARVs (because of side effects or drug resistance), they need to continue taking TDF with 3TC or FTC to avoid dangerous flares of HBV.

WHAT IS HCV

Hepatitis C is a virus that can cause serious, life-threatening liver damage.

In South Africa, an estimated 600,000 people have been infected with HCV, and 1-13% of the country's 7.7 million people living with HIV are co-infected with HCV.

Rates are much higher among people who inject drugs (up to 93% among people who inject drugs in Pretoria) and men who have sex with men.

HOW DO YOU GET HCV?

HCV is transmitted when blood from a person who is living with HCV enters another person's body, such as by:

- Sharing equipment to inject drugs that has been used by someone with HCV
- Condomless anal intercourse/ gloveless fisting among men who have sex with men, especially if they are living with HIV, and/or in the context of ChemSex (use of certain drugs during sex, often with multiple partners)
- Receiving an organ transplant or transfusion with unscreened blood or blood products, especially before 1992
- Vertical transmission during pregnancy, at delivery and up to 28 days after birth
- Undergoing medical or dental care with shared, unsterilised equipment that was used on a person with HCV
- Sharing tattooing needles, ink and inkwells with a person who has HCV
- Getting a piercing with unsterilised, shared needles
- Traditional scarification
- Circumcision with shared, unsterilised equipment
- Kidney dialysis with shared, unsterilised equipment
- Sharing straws/tubes for snorting cocaine
- Needlestick accidents and other occupational exposures to blood from a person with HCV
- Sharing personal care items that may have blood on them, such as razors, toothbrushes and manicuring implements.

HOW TO PREVENT HCV

There is no vaccine to prevent HCV, and a person can become infected with HCV over and over again – but there are ways that a person can protect themselves against HCV.

HCV can be prevented by:

- Scaling up access to harm reduction (including opioid substitution treatment and an ample supply of needles, syringes and all other injection equipment so people never have to share it)
- Using condoms with ample lubricant with each partner and gloves for fisting during ChemSex – and not sharing injection equipment
- Ensuring that medical, dental, tattooing/piercing, circumcision and traditional scarification equipment are sterilised after each use or only used once
- Offering women of childbearing potential HCV testing and treatment, if needed
- Providing personal equipment to each person in closed facilities and encouraging people not to share it
- Expanding access to HCV testing and treatment to all who need them.

WHAT HAPPENS TO PEOPLE WITH HCV?

HCV is not always a lifelong infection; some people have a strong immune response to that clears it without treatment, usually within six months of infection.

Overall, 15-45% of people with HCV alone, and 10% of people living with HIV clear HCV naturally; the rest develop a chronic infection.

If untreated, chronic HCV causes liver damage. As the immune system tries to protect uninfected liver cells from the virus by surrounding them, the liver becomes scarred. Once serious scarring, called cirrhosis, has developed, it can progress to liver failure or liver cancer.

The risk for liver damage from HCV is higher among:

- People living with HIV – liver damage is more likely, and happens faster, than in people with HCV alone – even when people are taking antiretroviral treatment (ART).
- People over age 40
- People who have had HCV for many years
- People who also have HBV
- Heavy drinkers – over 3 drinks of any kind (beer, wine or spirits) a day for women and over 4 drinks per day for men
- People who are obese
- Men

HCV also causes health problems outside of the liver, including pre-diabetes and type 2 diabetes, kidney and heart disease, skin problems, auto-immune disorders, depression, fatigue and difficulty with memory and concentration – and it can increase the risk for certain types of cancer.

HCV SYMPTOMS

Many people do not have symptoms after getting HCV. For those who do fall ill, the most common symptoms of a new HCV infection are:

- Fever
- Tiredness
- Appetite loss
- Nausea
- Vomiting
- Yellow skin and eyes
- Dark urine
- Grey colored stool

HCV often goes undiagnosed because people may not feel ill until many years later, when they have developed cirrhosis. The symptoms of cirrhosis include:

- Feeling weak and tired
- Having itchy skin
- Loss of appetite
- Nausea and vomiting
- Liver pain
- Yellow skin and eyes

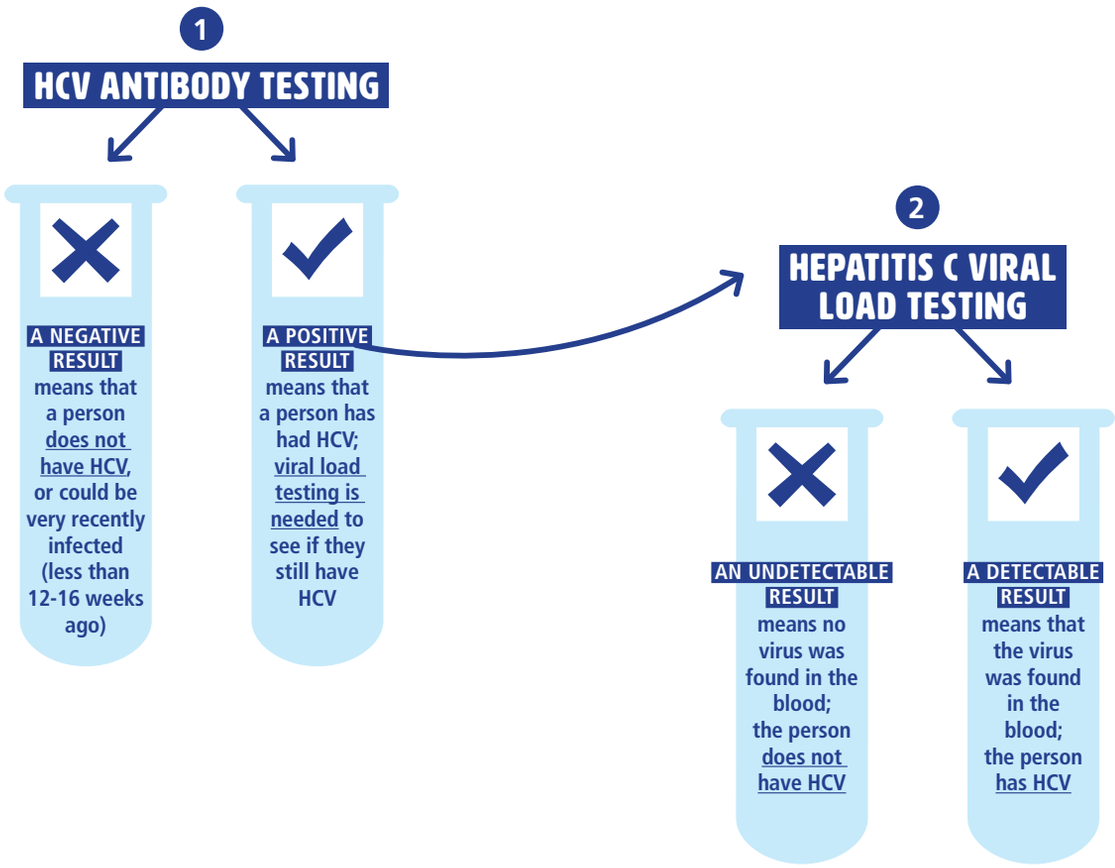
HCV TESTING

HCV testing is a two-step process, starting with a test for antibodies. With HCV, unlike HIV, a positive antibody test result does not mean that someone is currently infected – it means that at one point, HCV was in their body.

Because the immune system might have cleared HCV, people who test positive for HCV antibodies need a different test, called viral load, to see if HCV is still in their body.

Before starting HCV treatment, people need testing to see how much liver damage they have, since people with cirrhosis may need longer treatment. Liver damage can be measured by blood tests, or with a machine that measures liver stiffness using sound waves.

There are seven different genotypes, or families, of HCV. They were named with a number, in the order of their discovery. Each genotype has subtypes, which were named with a letter, in the order that they were discovered. Some DAAs work for all of them (called pan-genotypic) – if these are available, a pre-treatment genotype test is not needed. Genotyping may still be needed in places where HCV treatment options are limited.



HCV TREATMENT

The goal of HCV treatment is a cure – which lowers the risk of liver-related illness and death, improves quality of life, and prevents HCV from spreading. People who have an undetectable hepatitis C viral load 12 weeks after finishing DAA treatment are considered to be cured.

HCV is treated with a combination of DAAs from different classes, or families curing over 95% of people after 8–12 weeks of once-daily oral treatment. People who have an undetectable hepatitis C viral load 12 weeks after finishing DAA treatment are considered to be cured.

Table 2. DAAs by class

Name	Class	Pan-genotypic	Used in Combination in Combination With	Recommended in South African Guidelines	Recommended in WHO Guidelines
Daclatasvir (Dcv)	NS5A inhibitor	Yes	Sofosbuvir	Yes	Yes
Glecaprevir (G)	Protease inhibitor	Yes	Pibrentasvir	Yes	Yes
Ledipasvir (Ldv)	NS5A inhibitor	No	Sofosbuvir	Yes	No (except for adolescents age 12-17)
Pibrentasvir (P)	NS5A inhibitor	Yes	Glecaprivir	Yes	Yes
Sofosbuvir (Sof)	NS5B inhibitor	Yes	Daclatasvir or ledipasvir or velpatasvir	Yes	Yes
Velpatasvir (Vel)	NS5A inhibitor	Yes	Sofosbuvir	Yes	Yes

DAAs are just as likely to cure people who are HIV/HCV coinfected as those with HCV alone. Some DAAs cannot be used with certain ARVs, so people may need to switch their ARV regimen before starting HCV treatment.

Table 3. Interactions Between WHO-Recommended ARVs and DAAs

	Daclatasvir	Glecaprevir/ Pibrentasvir	Sofosbuvir	Velpatasvir
Dolutegravir				
Efavirenz	increase daclatasvir dose from 60 mg/day to 90 mg/day	Do not use together		Do not use together
Lopinavir/ Ritonavir		Do not use together		
Emtricitabine, Lamivudine, Tenofovir, Zidovudine				

DAAs have not been registered in South Africa yet, but they can be accessed through a SAHPRA (former Medicines Control Council [MCC]) Section 21 application process for named patients. Registration is expected in 2020 -2021.

APPENDIX

SOUTH AFRICAN HIV/HBV GUIDELINES

ART is recommended for everyone with HIV, at any CD4 cell count, including people with HBV. Before starting ART, HBsAg testing is recommended for all children, adolescents and adults, including pregnant women – but HIV treatment can be started before the results are available.

People who are living with HIV/HBV should be treated with a combination that includes TDF and FTC or 3TC. People who switch their ARVs should continue taking TDF with 3TC or FTC to avoid dangerous flares of HBV.

WORLD HEALTH ORGANIZATION (WHO) HIV/HBV GUIDELINES

WHO recommends ART for everyone with HIV, at any CD4 cell count, including people with HBV.

WHO recommends HBsAg testing before starting ART (if feasible); if it is not done before starting treatment, HBsAg testing should be done before switching treatment to ensure that people with HBV continue TDF.

People living with HIV and HBV should take the same first-line ARVs as people who are living with HIV – a regimen that includes TDF plus 3TC or FTC.

SOUTH AFRICAN HIV/HCV GUIDELINES

ART is recommended for all people living with HIV, at any CD4 cell count, including people with HCV co-infection. HCV treatment should be considered for all people living with HIV/HCV co-infection.

WHO HIV/HCV GUIDELINES

ART is recommended for all people living with HIV, at any CD4 cell count, including people with HCV co-infection.

WHO recommends HCV treatment with pan-genotypic DAAs for all people with chronic HCV over age 12.

Table 4. WHO-Recommended HCV Treatment

Regimen	All genotypes, no cirrhosis	All genotypes, cirrhosis
SOF/DCV	12 weeks	12 or 24 weeks
sofosbuvir/velpatasvir	12 weeks	12 weeks
glecaprevir/pibrentasvir	8 weeks	12 weeks

Source: WHO. Guidelines for the Care and Treatment of Persons Diagnosed With Chronic Hepatitis C Infection. 2018. Available from apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1

Table 5. South African HCV Treatment Guidelines

Genotype	No Cirrhosis	Duration	Cirrhosis	Duration
1a	Sofosbuvir/ Velpatasvir	12 Weeks	Sofosbuvir/ Velpatasvir	12 Weeks
	Sofosbuvir/ Ledipasvir	8 Or 12 Weeks	Sofosbuvir/ Ledipavir	12 Weeks
	Sofosbuvir/ Daclatasvir	12 Weeks	Sofosbuvir/ Daclatasvir	12 Weeks
	Glecaprevir/ Pibrentasvir	8 Weeks	Glecaprevir/ Pibrentasvir	12 Weeks
1b	Sofosbuvir/ Velpatasvir	12 Weeks	Sofosbuvir/ Velpatasvir	12 Weeks
	Sofosbuvir/ Ledipasvir	8 Or 12 Weeks	Sofosbuvir/ Ledipasvir	12 Weeks
	Sofosbuvir/ Daclatasvir	12 Weeks	Sofosbuvir/ Daclatasvir	12 Weeks
	Glecaprevir/ Pibrentasvir	8 Weeks	Glecaprevir/ Pibrentasvir	12 Weeks
2	Sofosbuvir/ Velpatasvir	12 Weeks	Sofosbuvir/ Velpatasvir	12 Weeks
	Sofosbuvir/ Daclatasvir	12 Weeks	Sofosbuvir/ Daclatasvir	12 Weeks
	Glecaprevir/ Pibrentasvir	8 Weeks	Glecaprevir/ Pibrentasvir	12 Weeks
3	Sofosbuvir/ Velpatasvir	12 Weeks	Sofosbuvir/ Velpatasvir	12 Weeks
	Sofosbuvir/ Daclatasvir	12 Weeks	Sofosbuvir/ Daclatasvir	12 Weeks
	Glecaprevir/ Pibrentasvir	8-12 Weeks	Glecaprevir/ Pibrentasvir	12-16 Weeks
4	Sofosbuvir/ Velpatasvir	12 Weeks	Sofosbuvir/ Velpatasvir	12 Weeks
	Sofosbuvir/ Ledipasvir (with or without weight-based ribavirin)	12 Weeks	Sofosbuvir/ Ledipasvir (with weight-based ribavirin)	12 Weeks
	Sofosbuvir/ Daclatasvir	12 Weeks	Sofosbuvir/ Daclatasvir	12 Weeks
	Glecaprevir/ Pibrentasvir	8 Weeks	Glecaprevir/ Pibrentasvir	12 Weeks
5	Sofosbuvir/ Velpatasvir	12 Weeks	Sofosbuvir/ Velpatasvir	12 Weeks
	Sofosbuvir/ Ledipasvir	12 Weeks	Sofosbuvir/ Ledipasvir	12 Weeks
	Sofosbuvir/ Daclatasvir	12 Weeks	Sofosbuvir/ Daclatasvir	12 Weeks
	Glecaprevir/ Pibrentasvir	8 Weeks	Glecaprevir/ Pibrentasvir	12 Weeks

Source: Department of Health, Republic of South Africa. National Guidelines for the Management of Viral Hepatitis. 2019. Available from sahivsoc.org/Files/SA%20NDOH_Viral%20Hepatitis%20guideilnes%20final_.pdf

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Q AND A

1. WHAT DOES THE LIVER DO?

The liver is the body's filter and processing plant. Everything a person eats and drinks, all the medicines they take, including antiretrovirals (ARV), and even the air they breathe passes through it.

2. WHAT CAUSES HEPATITIS?

Hepatitis means swollen liver. Different things can cause it: exposure to toxic fumes, taking certain medicines, drinking large amounts of alcohol and bacterial or viral infections.

3. DOES HIV MAKE VIRAL HEPATITIS WORSE?

Yes, HIV increases the risk and speeds up the rate of liver damage from viral hepatitis.

4. HOW DOES A PERSON GET HEPATITIS B VIRUS (HBV)?

HBV is transmitted by body fluids (blood, semen, vaginal fluid and saliva). HBV can be vertically transmitted, and passed by condomless anal, vaginal and oral sex, injecting drugs with shared and unsterilized equipment, undergoing medical or dental procedures with unsterilized equipment, being tattooed with shared needles, ink and inkwells, and via traditional scarification practices, female genital mutilation, needlestick accidents and sharing razors, toothbrushes and manicuring equipment.

5. IS THERE A VACCINE TO PREVENT HBV?

Yes — it is a series of three vaccines.

6. CAN HBV BE TREATED IN PEOPLE WHO ARE LIVING WITH HIV?

Some ARVs work against HIV and HBV. People who are living with HIV/HBV should be treated with a combination that includes tenofovir (TDF) with emtricitabine (FTC) or lamivudine (3TC).

7. HOW DOES A PERSON GET HCV?

HCV is transmitted when blood from someone who has HCV directly enters another person's body. People can get HCV from injecting drugs with shared equipment, undergoing dental or medical care, including dialysis, with shared, unsterilised equipment or getting a transfusion before 1992; through vertical transmission and by sharing tattooing needles, ink and inkwells; piercing with an unsterilised, shared needle; condomless anal intercourse/ gloveless fisting among men who have sex with men; via traditional scarification or circumcision with shared, unsterilised equipment; snorting cocaine with a shared straw or note; needlestick accidents and other occupational exposures to blood, and from sharing personal care items that may have blood on them, such as razors, toothbrushes and manicuring implements.

8. IS THERE A VACCINE TO PREVENT HCV?

No.

9. DOES A POSITIVE ANTIBODY TEST RESULT MEAN THAT A PERSON HAS HCV?

No. A positive antibody test result means that someone was infected with HCV at one time. Their immune system may have cleared the virus; they need a different test that looks for the actual hepatitis C virus to see if they are currently infected.

10. CAN HCV BE TREATED IN A PERSON LIVING WITH HIV?

A 12-week course of once-daily, oral HCV treatment will cure over 95% of people – and it works just as well for people living with HIV as it does for people with HCV alone.

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