Professional Information For:

HEP B VACCINE PAED CIPLA

HEP B VACCINE ADULT CIPLA

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

HEP B VACCINE PAED CIPLA

(10 mcg Purified Hepatitis B surface antigen per 0,5 mL, suspension for injection)

HEP B VACCINE ADULT CIPLA

(20 mcg Purified Hepatitis B surface antigen per 1 mL, suspension for injection)

2.QUALITATIVE AND QUANTITATIVE COMPOSITION

HEP B VACCINE PAED CIPLA:

Each 0,5 mL contains 10 mcg Purified Hepatitis B surface antigen adsorbed on aluminium hydroxide

(Al^{+++}) 0,25 mg to 0,40 mg.

Preservative: Thiomersal 0,005 % *m/v*

Sugar free

HEP B VACCINE ADULT CIPLA:

Each 1 mL contains 20 mcg Purified Hepatitis B surface antigen, adsorbed on aluminium hydroxide

(Al^{+++}) 0,50 mg to 0,80 mg.

Preservative: Thiomersal 0,005 % *m/v*

Sugar free

For full list of excipients, (**see section 6.1**)

3. PHARMACEUTICAL FORM

HEP B VACCINE PAED CIPLA suspension for injection:

White turbid suspension in which mineral carrier tends to settle down slowly when stored.

HEP B VACCINE ADULT CIPLA suspension for injection:

White turbid suspension in which mineral carrier tends to settle down slowly when stored.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

HEP B VACCINE CIPLA is used for active immunisation against hepatitis B infection.

Immunisation against hepatitis B is expected in the long term to reduce not only the incidence of this disease, but also its chronic complications such as chronic active hepatitis B and hepatitis B associated cirrhosis and primary hepatocellular carcinoma.

In areas of low prevalence of hepatitis B, immunisation with HEP B VACCINE CIPLA is recommended for neonates/infants and adolescents as well as for subjects who are, or will be, at increased risk of infection such as:

- healthcare personnel, laboratory workers, or any other personnel who have direct contact with patients or their body fluids or tissues,
- patients with chronic renal failure including those requiring haemodialysis,
- haemophiliacs and those receiving regular blood transfusions or blood products,

- close family contacts or sexual partners of cases or carriers of hepatitis B,
- persons at increased risk due to their sexual behaviour,
- parenteral drug abusers,
- travellers to areas where hepatitis B is endemic,
- infants born to women who are persistent carriers of hepatitis B surface antigen or infants born to women who are HBsAg-positive as a result of recent infection,
- others: police personnel, fire brigade personnel, armed forces personnel and anybody who through their work or personal lifestyle may be exposed to Hepatitis B vaccine (HBV),
- household contacts of any of the above groups and of patients with acute or chronic HBV
  infection.

In areas of intermediate or high prevalence of hepatitis B, with most of the population at risk of acquiring the disease, immunisation should be offered to all neonates and young children. Immunisation should also be considered for adolescents and young adults.

4.2 Posology and method of administration

Posology:

Neonates, infants, and younger children:

A dose of 10 mcg of antigen protein in 0,5 mL suspension for injection is recommended for neonates, infants, children, and adolescents up to 19 years of age.

Adults:

A dose of 20 mcg of antigen protein in 1 mL suspension for injection is recommended for adults aged 20 years and above.

Immunisation schedule

Primary immunisation: A series of three intramuscular injections is required to achieve optimal protection.

The following immunisation schedules can be recommended:

- 6, 10, 14 weeks for infants,
- 0, 1, 6 months,
- 0, 1, 2 months (rapid schedule).

Booster dose

The need for the booster dose in healthy individuals, who have received the full primary immunisation, is not recommended. It would seem advisable to recommend a booster dose when Anti-HBs antibody titres fall below 10 IU/L for all people at risk and especially for patients who are immune compromised (HIV infected patients) or those on haemodialysis.

Special Populations:

Dosage recommendation for neonates born of mothers who are HBV carriers

The 0, 1, 2 month immunisation schedule is recommended, and should start at birth. Concomitant administration of Hepatitis B immunoglobulin not necessary, but when Hepatitis B immunoglobulin is given simultaneously with Hepatitis B vaccine a separate injection site must be chosen.

D*osage recommendation for known or presumed exposure of HBV*

In circumstances where exposure to HBV has recently occurred (e.g., needle stick with contaminated needle) the first dose of HEP B VACCINE CIPLA can be administered simultaneously with Hepatitis B immunoglobulin which, however, must be given at a separate injection site. The rapid immunisation schedule should be advised.

D*osage recommendation for immunocompromised persons*

The primary immunisation schedule for chronic haemodialysis patients or persons who have an impaired immune system is four doses of 40 mcg at 0, 1, 2 and 6 months from the date of first dose. The immunisation schedule should be adapted in order to ensure that the anti-HBs antibody titre remains above the accepted protective level of 10 IU/L.

Method of administration

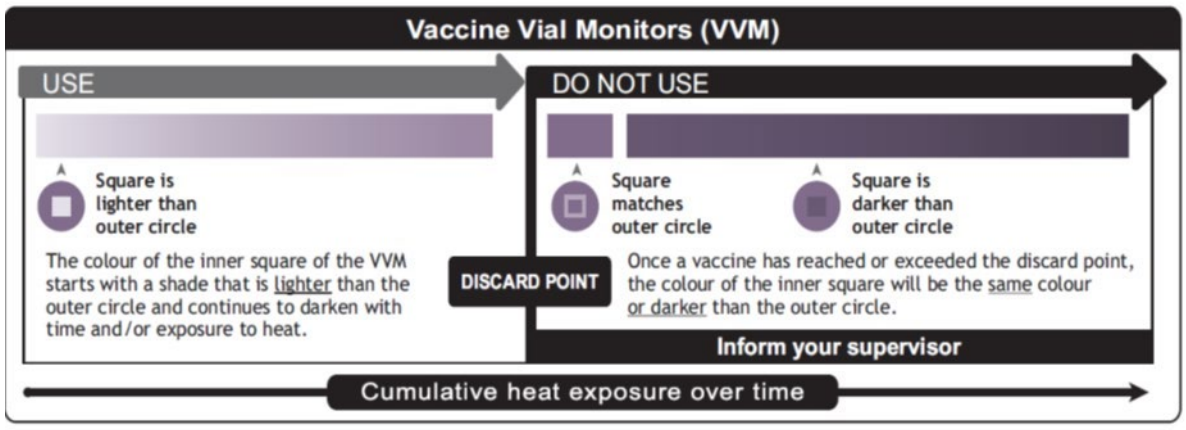
HEP B VACCINE CIPLA should be injected intramuscularly in the deltoid region in adults and children or in the anterolateral thigh in neonates, infants and young children. HEP B VACCINE CIPLA may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders.

The vaccine should be well shaken before use. Only sterile needle and syringes should be used for each injection. Once opened, multi-dose vials should be kept between + 2 °C and + 8 °C.

Multi-dose vials of HEP B VACCINE CIPLA from which one or more doses of vaccine have been removed during an immunisation session may be used in subsequent immunisation sessions for up to a maximum of 28 days, provided that all of the following conditions are met:

- The expiry date has not passed;
- The vaccines are stored under appropriate cold chain conditions;
- The vaccine vial septum has not been submerged in water;
- Aseptic technique has been used to withdraw all doses;
- The vaccine vial monitor (VVM), if attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

The vaccine should be visually inspected for any foreign particulate matter and/or variation of physical aspect prior to administration. In event of either being observed, discard the vaccine.



4.3 Contraindications

HEP B VACCINE CIPLA should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous Hepatitis B vaccine administration.

4.4 Special warnings and precautions for use

HEP B VACCINE CIPLA should not be administered in the gluteal region or intradermally since these routes of administration may not result in an optimum immune response.

HEP B VACCINE CIPLA should never be administered intravenously.

Because of the long incubation period of hepatitis B it is possible for unrecognised infection to be present at the time of vaccination. HEP B VACCINE CIPLA may not prevent hepatitis B in such cases. HEP B VACCINE CIPLA will not prevent infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E and other pathogens known to infect the liver.

In haemodialysis patients and persons with an impaired immune system, adequate anti-HBs antibody titres may not be obtained after the primary immunisation course and such patients may therefore require administration of additional doses of vaccine (**see Section 4.2**).

As with all injectable vaccines, appropriate medication (e.g., adrenaline) should always be readily available for treatment in case of rare anaphylactic reactions following the administration of HEP B VACCINE CIPLA.

The immune response to hepatitis B vaccines is related to age. In general, people over 40 years of age respond less well.

HEP B VACCINE CIPLA may be used to complete a primary immunisation course started either with plasma-derived or with other genetically engineered hepatitis B vaccines, or as a booster dose in subjects who have previously received a primary immunisation course with plasma-derived or with other genetically engineered hepatitis B vaccines.

Hepatitis B vaccine may be administered to HIV infected people, both asymptomatic and symptomatic and as early as possible according to national guidelines for vaccination of HIV patients (**see Section 4.2**).

4.5 Interaction with other medicines and other forms of interaction

The vaccine can be safely and effectively given simultaneously but at different injection site with DTP, DT, TT, BCG, Measles, Polio vaccine (OPV and IPV) and yellow fever vaccine. It should not be mixed in the vial or syringe with any other vaccine unless it is manufactured as a combined product (e.g., DTPHep B).

4.6 Pregnancy and lactation

Pregnancy

The safety of HEP B VACCINE CIPLA in pregnancy has not been established.

Breast-feeding

The safety of HEP B VACCINE CIPLA in lactation has not been established.

4.7 Effects on ability to drive and use machines

HEP B VACCINE CIPLA has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a) Summary of the safety profile

The undesirable events are temporally related to the administration of Hepatitis B vaccine. They are usually mild and confined to the first few days of the vaccination. The

most common reactions are mild soreness, erythema, induration, fatigue, fever, malaise, influenza-like symptoms

Less common systemic reactions include nausea, vomiting, diarrhoea, abdominal pain, abnormal liver function tests, arthralgia, myalgia, rash, pruritus, urticaria.

b) Tabulated (or structured listing) summary of adverse reactions

The following adverse events were reported in clinical trials of the Hepatitis B Vaccine (rDNA), irrespective of causal association.

Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), or very rare (<1/10,000), and not known (cannot be estimated from the available data).

System Organ Class	**Adverse drug reactions**
Infections and Infestations	
Uncommon	Upper respiratory tract infection
Rare	Nasopharyngitis
Nervous system disorders	
Uncommon	Headache, dizziness
Rare	Somnolence
Vascular disorders	
Rare	Flushing
Gastrointestinal disorders	

Common	Nausea
Rare	Abdominal pain
Hepatobiliary disorders	
Rare	Jaundice
Skin and subcutaneous tissue disorders	
Rare	Rash, pruritus
Musculoskeletal and connective tissue disorders	
Uncommon	Myalgia, arthralgia
General disorders and administration site conditions	
Common	Injection site pain, Injection site swelling, pyrexia
Uncommon	Injection site erythema, injection site induration, injection site nodule, malaise
Rare	Injection site pruritis, injection site rash, injection site discoloration, body ache

4.9 Overdose

No case of overdose has been reported. Treatment of adverse effects is symptomatic and supportive (**see Section 4.8 and Section 4.4**)

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: A 30.1 Vaccine Antigens

ATC code: J07BC01

Mechanism of Action:

Hepatitis B vaccine (recombinant) stimulates active immunity to hepatitis B virus (HBV) infection. Immunisation to hepatitis B virus infection appears in most of the subjects having received three doses of hepatitis B vaccine for any of the vaccination schedules used.

Hepatitis-B surface antigen (HBsAg), which is present in hepatitis B vaccine (recombinant), promotes the production of antibody to HBsAg (anti-HBs); anti-HBs neutralises the HBV so that its infective or pathogenic properties are inhibited. Administration of hepatitis B vaccine (recombinant) during the incubation period of infection (i.e., after exposure to hepatitis B virus but prior to onset of clinical symptoms) may only modify or ameliorate, rather than prevent infection.

The active immune response produced by hepatitis B vaccine (recombinant) does not appear to be suppressed by hepatitis B immune globulin (HBIG) when HBIG is administered concomitantly at separate sites.

Immunological Data:

Various clinical trials performed to assess Immunogenicity and reactogenicity of the vaccine proved that the vaccine is immunogenic.

In a Phase III clinical trial in Chennai, India; in 64 adults aged 18-60 years, administration of Hepatitis B vaccine, in a dose of 1 mL in 0,1,2 month schedule, seroconversion was 100 % and seroprotection was 98,43 %.

In a comparative phase III clinical trial in Hyderabad, India, 160 adults were equally randomised to receive Genevac-B or Shanvac-B in a dose of 1 mL at 0,1,6 months. Seroconversion and seroprotection was 100 % in both groups.

Boosters

Refer to **section 4.2** on booster dose.

Microbiology:

Hepatitis B vaccine (rDNA) is a non-infectious recombinant DNA hepatitis B vaccine. It contains purified surface antigen of the virus obtained by culturing genetically engineered *Hansenula polymorpha* yeast cells having the surface antigen gene of the hepatitis B virus. The hepatitis B surface antigen (HBsAg) expressed in the cells of *Hansenula polymorpha* is purified through several chemical steps and formulated as a suspension of the antigen adsorbed on aluminium hydroxide and thiomersal is added as preservative.

5.2. Pharmacokinetic properties

Not relevant for vaccines.

6 PHARMACEUTICAL PARTICULARS

6.1. List of excipients Aluminium hydroxide gel, Thiomersal, **Phosphate buffer** composed of: Water for injection, disodium hydrogen phosphate anhydrous, sodium chloride, sodium dihydrogen phosphate dihydrate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months when stored at + 2 °C to + 8 °C.

For multidose vials: once the vial has been opened it should be stored at + 2 °C to + 8 °C for not more than 28 days (**see section 4.2**)

6.4. Special precautions for storage

HEP B VACCINE CIPLA should be stored in a refrigerator at + 2 °C to + 8 °C. DO NOT FREEZE.

Discard if vaccine has been frozen.

Keep the product in the carton until ready for use.

6.5. Nature and contents of container

HEP B VACCINE PAED CIPLA:

0,5 mL - Single dose 4 mL type I glass vial packed into single unit cartons, carton of 10 vials or carton of 50 vials.

The vial is closed with a grey bromo-butyl rubber stopper, and an aluminium seal having a blue coloured flip-off cap.

5 mL - 10 doses 5 mL type I glass vial packed into carton of 10 vials or carton of 50 vials. The vial is closed with a grey bromo-butyl rubber stopper and an aluminium seal having a blue coloured flip-off cap.

Not all pack sizes may be marketed.

HEP B VACCINE ADULT CIPLA:

1 mL - Single dose 4 mL type I glass vial packed into single unit cartons, carton of 10 vials or carton of 50 vials.

The vial is closed with a grey bromo-butyl rubber stopper and an aluminium seal having a blue coloured flip-off cap.

10 mL - 10 doses 15 mL type I glass vial packed into carton of 25 vials.

The vial is closed with a grey bromo-butyl rubber stopper and an aluminium seal having a blue coloured flip-off cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements**.**

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBERS

HEP B VACCINE PAED CIPLA: 48/30.1/0376

HEP B VACCINE ADULT CIPLA: 48/30.1/0375

9. DATE OF FIRST AUTHORISATION

25 August 2020

10. DATE OF REVISION OF THE TEXT

March 2022