Hepavax-Gene® TF inj.

Hepatitis B Vaccine (rDNA), Thimerosal-Free

Product name

Hepavax Gene TF-Suspension for injection, Hepatitis B (rDNA) vaccine (adsorbed)
20 micrograms / 1.0 mL (Adult)
10 micrograms / 0.5mL(Pediatric)

Composition

One dose for adults contains:
Hepatitis B virus surface antigen, recombinant (HBsAg): 20 micrograms, adsorbed on 500 micrograms aluminium hydroxide gel (as Al***).
One pediatric dose contains:
Hepatitis B virus surface antigen, recombinant (HBsAg): 10 micrograms, adsorbed on 250 micrograms aluminium hydroxide gel (as Al***).

Pharmaceutical Form Suspension for injection, Visual form: slightly opaque, white suspension

Indications

The vaccine is indicated for active immunization against hepatitis B virus infection.
It is expected that vaccination against hepatitis B protects from hepatitis D as well, as hepatitis D infection occurs only in the presence of hepatitis B.
The vaccine may be used in accordance with National Immunization Program.
The vaccination is recommended especially for those who are, or will be, at risk of exposure to infections with hepatitis B virus, for example:

- Medical staff: surgeons, dentists, doctors, nurses, assisting staff, hemodialysis, hematology, oncology wards personnel, laboratory and other personnel having contact with blood and other blood products, blood bank workers, funeral workers, beauticians, emergency personnel etc.
- Patients: Patients with transfusions or recipients of blood components such as hemodialysis and oncology wards patients, patients with sickle cell anemia, liver cirrhosis, hemophilia etc.
- Personnel and residents of confined institutions (nursing houses, prisons, etc).
- Persons having frequent or/and close contact with high risk groups: prisoners, guards, other prison employees.
- Persons at high risk due to sexual practices.
- Drug addicts.
- Travelers going to regions with high infection risk and persons having close contact with them.
- Family members of the groups mentioned above and family members of patients with acute hepatitis.
- Neonates of HBsAg infected mothers.
- Soldiers and other personnel in active service, who are at risk of the infection.

In the areas of medium and high endemicity all children, neonates and adults from high risk groups should be vaccinated.
It is expected that vaccination against hepatitis B will not only reduce the number of infections in the future but also will reduce the occurrence of complications such as chronic hepatitis, liver cirrhosis, and primary liver cancer.

Dosage and Administration

Dosage

Adult and adolescent populations

Adults and adolescents (above 15 years of age): 1 dose of 1.0 mL (20 micrograms) is intended for use.

Pediatric populations

Neonates and children up to 15 years of age: 1 dose of 0.5 mL (10 micrograms) is intended for use.

Administration

Hepavax-Gene® TF should be injected intramuscularly into the deltoid muscle in older children and adults or in the anterolateral thigh in neonates, infants and young children. There is no experience with the subcutaneous mode of administration. In patients with severe bleeding tendencies (e.g. hemophilia, thrombocytopenia) an exception can be made on the route of administration by injecting the vaccine subcutaneously.

Administration schedule:

Standard course of vaccination :

The vaccination regimen for all subjects without any condition impairing the immune response consists of 3 doses of vaccine given at 0, 1, and 6 months. Once initiated, this primary course of vaccination is recommended to be completed with Hepavax-Gene® TF.

Accelerated course of vaccination:

For a more rapid onset of protection, the accelerated course consists of 3 injections given at 0, 1, and 2 months. Once initiated, this primary course of vaccination is recommended to be completed with Hepavax-Gene® TF. For optimal protection, a booster dose, 12 months after the first injection, is recommended.

Special administration schedule recommendations:

Neonates of mothers who are hepatitis B virus carriers:

- One dose of hepatitis B immunoglobulin (HBIG) should be given at birth (within 24 hours)
- The first vaccine dose should be given within 7 days of birth.
  - o It is preferable to administer the first vaccine dose simultaneously with HBIG, but at separate injection sites.
- Subsequent doses of the vaccine should be given according to the locally recommended vaccination schedule.

Known or presumed exposure to hepatitis B virus (e.g. needle stick with contaminated needle):

- HBIG should be given as soon as possible after exposure (within 24 hours)
- The first vaccine dose should be given within 7 days of exposure.
  - o It is preferable to administer the first vaccine dose simultaneously with HBIG, but at separate injection sites
- Subsequent vaccine doses, if necessary (depending on the serologic status of the patient), should be given as in the recommended immunization schedule. The accelerated schedule can be proposed.

Boosting after successful vaccination

As with other hepatitis B vaccines, the duration of the protective effect of Hepavax-Gene® TF in healthy vaccinees is unknown at present and the need for a booster dose is not yet defined. However, some local vaccination schedules currently include a recommendation for a booster dose. In general, the administration of a booster dose should be based on official local guidance.
Antibody levels of subjects at risk can be assessed at regular intervals and appropriate boosters administered when titers fall below minimal protective levels (< 10 IU/L).

Contraindications

Hepavax-Gene® TF should not be administered to subjects with known hypersensitivity to the active substance or any of the excipients of the vaccine or to subjects who developed symptoms suggestive of hypersensitivity after the injection of Hepavax-Gene® TF.
As with other vaccines, the administration of Hepavax-Gene® TF should be postponed in subjects suffering from acute severe illness and acute febrile infections. The presence of a minor infection, however, is not a contraindication for immunization.

Warnings and Precautions

Due to the long incubation period for hepatitis B, it is possible for unrecognized infection to be present at the time of vaccination. Vaccination may not prevent hepatitis B in such individuals.
The vaccine will not prevent hepatitis caused by other agents such as hepatitis A, hepatitis C and hepatitis E or other pathogens known to infect the liver.
The immune response to hepatitis B vaccines may be reduced by several factors such as older age (> 40 years), obesity and smoking habits. The response may be reduced also in patients with dialysis and immunological disorders. In populations affected by these factors, an impaired immune response to primary vaccination is possible, and additional doses or booster vaccinations may be needed.
As with all injectable vaccines, appropriate medical treatment should always be readily available in case of a rare anaphylactic shock following the administration of the vaccine. The subjects should be monitored by a healthcare professional for 30 minutes after vaccination
Syncope (fainting) can occur in association with administration of injectable vaccines. Syncope can be accompanied by falls. Procedures should be in place to avoid falling injury. If syncope develops, individuals should be observed until the symptoms resolve.
Vaccination into the gluteal area or intracutaneous/intradermal administration should be avoided since this could lead to a suboptimal response to the vaccine.
HEPAVAX-GENE® TF SHOULD NOT BE ADMINISTERED INTRAVASCULARLY.
Excipients:
This medical product contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium free'.
This medicinal product contains sodium, less than 1 mmol (23 mg) per dose, i.e. essentially 'sodium free'.

Interactions

Hepavax-Gene® TF can be administered concomitantly with other vaccines according to the National Immunization Program. If administered concomitantly, the different vaccines should be given with different syringes and injected at different sites.
Hepavax-Gene® TF can be administered with HBIG, and should be administered at a separate injection site with a separate syringe.
As clinically shown, Hepavax-Gene® TF can be used for completing a primary immunization course started with other hepatitis B vaccines or as a booster dose.
In patients undergoing immunosuppressive therapy, immune response to the vaccine may be impaired.

Pregnancy, Breast feeding and Fertility

Pregnancy

There are no adequate data from the use of Hepavax-Gene® TF in pregnant women. There are limited data in animals on the effects on pregnancy, embryonal and fetal development, parturition and postnatal development (see Non-Clinical Information). There is no evidence of risk to the fetus. However, Hepavax-Gene® TF should only be used during pregnancy when there is a clear risk of hepatitis B infection and when the benefit outweighs the risk.

Breast feeding

It is unknown whether Hepavax-Gene® TF is excreted in human breast milk. The excretion of Hepavax-Gene® TF in milk has not been studied in animals. Hepavax-Gene vaccine is a recombinant vaccine. Recombinant vaccines are considered to pose no risk for mothers who are breast feeding or for their infants.

However, Hepavax-Gene® TF should be administered during breast feeding only when there is a clear risk of hepatitis B infection and when the benefit outweighs the risk.

Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed.

Adverse Reactions

Throughout this section, adverse reactions are presented. Adverse reactions are adverse events that were considered to be reasonably associated with the use of Hepavax-Gene® and Hepavax-Gene® TF based on the comprehensive assessment of the available adverse event information. A causal relationship with Hepavax-Gene® and Hepavax-Gene® TF cannot be reliably established in individual cases. Further, because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

The safety assessment is based on all safety data from 847 healthy adults (2219 doses) and 1688 healthy children and neonates (5013 doses) administered Hepavax-Gene® or Hepavax-Gene® TF in four clinical studies. Hepavax-Gene® and Hepavax-Gene® TF are generally well tolerated. No serious adverse reactions attributable to the vaccine have been reported during the course of these clinical studies. As with any vaccine, there is the possibility that broad use of the vaccine could reveal adverse reactions not observed in clinical studies. Both injection site and systemic adverse reactions were generally transient (2 3 days) and mild to moderate. The reported adverse reactions were comparable with those seen with other hepatitis B vaccines.

The incidences of adverse reactions observed in clinical studies with the vaccine are presented in Table 1 (adult subjects) and Table 2 (pediatric subjects). Adverse reactions are listed by system organ class and frequency: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1000 to < 1/100), and rare (≥ 1/10000 to < 1/1000). Due to the number of subjects assessed in the current analysis of Hepavax Gene and Hepavax-Gene® TF studies, single incidences fall into the category "rare". Within each frequency category, adverse reactions are presented in order of decreasing frequency.

Adult subjects:

For adult subjects, the most common injection site reactions were: pain (28.5%), itching (4.1%), and erythema (2.4%).

The most common systemic reactions were: fatigue (14.6%), myalgia (13.9%), and malaise (8.3%). Fever (≥38˚C) was reported in 1% of adult subjects.

Pediatric subjects:

For pediatric subjects, the most common injection site reactions were: erythema (2.8%), induration (1.9%), swelling (1.5%), and pain (1.4%).

The most common systemic reactions were: fever (≥ 38˚C; 3.6%), and crying (2.8%).

Table 1: Adverse reactions with Hepavax-Gene® or Hepavax-Gene® TF observed in clinical studies in adult subjects

System Organ Class	
Frequency Category	Adverse Reaction
Nervous System Disorders	
Uncommon:	headache
Rare:	dizziness, somnolence
Vascular Disorders	
Rare:	hypotension
Respiratory, Thoracic and Mediastinal Disorders	
Rare:	rhinitis[a]
Gastrointestinal Disorders	
Uncommon:	nausea,vomiting abdominal pain, diarrhea
Rare:	stomatitis
Skin and Subcutaneous Tissue Disorders	
Common:	rash, pruritis
Musculoskeletal and Connective Tissue Disorders	
Very common:	myalgia
Common:	arthralgia
General Disorders and Administration Site Conditions	
Very common:	injection site pain, fatigue
Common:	malaise injection site pruritus injection site erythema injection site swelling fever (≥38°C)
Uncommon:	pyrexia[b] influenza like illness[a]
Rare:	injection site burning

[a] from study GCVC5 and GCVC11

[b] preferred term refers to any clinically significant increase in body temperature reported as an unsolicited adverse event by the investigator

Table 2: Adverse reactions with Hepavax-Gene® or Hepavax-Gene® TF observed in clinical studies in pediatric subjects

System Organ Class	
Frequency Category	Adverse Reaction
Infections and Infestations	
Common:	nasopharyngitis
Blood and Lymphatic System Disorders	
Rare:	lymphadenopathy
Immune System Disorders	
Uncommon:	allergic reaction
Metabolism and Nutrition Disorders	
Uncommon:	feeding disorder
Rare:	anorexia
Psychiatric Disorders	
Uncommon:	mental status changes
Nervous System Disorders	
Uncommon:	headache
Rare:	convulsions, somnolence
Respiratory, Thoracic and Mediastinal Disorders	
Uncommon:	cough, rhinorrhea
Gastrointestinal Disorders	
Common: Uncommon:	vomiting diarrhea, nausea, abdominal distension, dyspepsia(including infantile spitting up)
Rare:	abdominal pain
Skin and Subcutaneous Tissue Disorders	
Uncommon:	rash (including pustular rash), eczema, mucous membrane disorder
Rare:	pruritus, urticaria
Musculoskeletal and Connective Tissue Disorders	
Rare:	myalgia
General Disorders and Administration Site Conditions	
Common:	fever (≥38°C), pyrexia[a], crying, injection site erythema, induration, injection site swelling, injection site pain
Uncommon:	altered activity level, fatigue

[a] preferred term refers to any clinically significant increase in body temperature reported as an unsolicited adverse event by the investigator

Postmarketing data In postmarketing reports, hypersensitivity reactions, including oedema and angioedema, were observed with unknown frequencies (cannot be estimated from the available data).

Overdose No case of overdose in humans has been reported. No serious adverse reactions are expected to result from overdose with Hepavax-Gene® TF.

List of Excipients Disodium phosphate dodecahydrate / Potassium dihydrogenphosphate / Sodium chloride / Water for injection

STORAGE Store refrigerated between 2 to 8˚C. Do not freeze. **Keep reach out of children.**

SHELF LIFE The shelf-life of Hepavax-Gene® TF inj. is 36 months from the date of manufacture when stored at 2 to 8˚C. The expiry date is shown on the label.

HOW SUPPLIED

As a single dose vial of vaccine:

10mcg/0.5mL vial × in house packaging unit. 20mcg/1.0mL vial × in house packaging unit.

The vaccine vial monitor

Vaccine Vial Monitors (VVMs) are part of the label on Hepavax-Gene® TF inj. supplied through Janssen Vaccines Corp.. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

Manufacturer

Janssen Vaccines Corp.

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Product registration holder, Importer and Distributor

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