

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fendrix suspension for injection
Hepatitis B (rDNA) vaccine (adjuvanted, adsorbed).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml) contains:

Hepatitis B surface antigen ^{1, 2, 3}	20 micrograms
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¹ adjuvanted by AS04C containing: - 3- <i>O</i> -desacyl-4'-monophosphoryl lipid A (MPL) ²	50 micrograms
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²adsorbed on aluminium phosphate (0.5 milligrams Al³⁺ in total)

³produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection.

Turbid white suspension. Upon storage, a fine white deposit with a clear colourless supernatant can be observed.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fendrix is indicated in adolescents and adults from the age of 15 years onwards for active immunisation against hepatitis B virus infection (HBV) caused by all known subtypes for patients with renal insufficiency (including pre-haemodialysis and haemodialysis patients).

4.2 Posology and method of administration

Posology

Primary immunisation:

The primary immunisation consists of 4 separate 0.5 ml doses administered at the following schedule: 1 month, 2 months and 6 months from the date of the first dose.

Once initiated, the primary course of vaccination at 0, 1, 2 and 6 months should be completed with Fendrix, and not with other commercially available HBV vaccine.

Booster dose:

As pre-haemodialysis and haemodialysis patients are particularly exposed to HBV and have a higher risk to become chronically infected, a precautionary attitude should be considered i.e. giving a booster

dose in order to ensure a protective antibody level as defined by national recommendations and guidelines.

Fendrix can be used as a booster dose after a primary vaccination course with either Fendrix or any other commercial recombinant hepatitis B vaccine.

Special posology recommendation for known or presumed exposure to HBV:

Data on concomitant administration of Fendrix with specific hepatitis B immunoglobulin (HBIG) have not been generated. However, in circumstances where exposure to HBV has recently occurred (e.g. stick with contaminated needle) and where simultaneous administration of Fendrix and a standard dose of HBIG is necessary, these should be given at separate injection sites.

Paediatric population

The safety and efficacy of Fendrix in children aged less than 15 years have not been established.

Method of administration

Fendrix should be injected intramuscularly in the deltoid region.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypersensitivity after previous administration of other hepatitis B vaccines.

The administration of Fendrix should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection such as a cold, is not a contraindication for immunisation.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

Because of the long incubation period of hepatitis B, it is possible that subjects could have been infected before the time of immunisation. The vaccine may not prevent hepatitis B infection in such cases.

The vaccine will not prevent infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E or other pathogens known to infect the liver.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

A number of factors have been observed to reduce the immune response to hepatitis B vaccines. These factors include older age, male gender, obesity, smoking, route of administration, and some chronic underlying diseases. Consideration should be given to serological testing of those subjects who may be at risk of not achieving seroprotection following a complete course of Fendrix. Additional doses may need to be considered for subjects who do not respond or have a sub-optimal response to a course of vaccinations.

Since intramuscular administration into the gluteal muscle could lead to a suboptimal response to the vaccine, this route should be avoided.

Fendrix should under no circumstances be administered intradermally or intravenously.

Patients with chronic liver disease or with HIV infection or hepatitis C carriers should not be precluded from vaccination against hepatitis B. The vaccine could be advised since HBV infection can be severe in these patients: the Hepatitis B vaccination should thus be considered on a case-by-case basis by the physician.

Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interaction

No data on the concomitant administration of Fendrix and other vaccines or with specific hepatitis B immunoglobulin have been generated. If concomitant administration of specific hepatitis B immunoglobulin and Fendrix is required, these should be given at different injection sites. As no data are available for the concomitant administration of this particular vaccine with other vaccines, an interval of 2 to 3 weeks should be respected.

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of Fendrix in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Vaccination during pregnancy should only be performed if the risk-benefit ratio at individual level outweighs possible risks for the foetus.

Breast-feeding

There are no data from use of Fendrix during lactation. In a reproductive toxicity study in animals which included post-natal follow-up until weaning (see section 5.3), no effect on the development of the pups was observed. Vaccination should only be performed if the risk-benefit ratio at individual level outweighs possible risks for the infant.

Fertility

No fertility data are available.

4.7 Effects on ability to drive and use machines

Fendrix has moderate influence on the ability to drive and use machine.

Some of the undesirable effects mentioned under section 4.8 may affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Clinical trials involving the administration of 2,476 doses of Fendrix to 82 pre-haemodialysis and haemodialysis patients and to 713 healthy subjects ≥ 15 years of age allowed to document the reactogenicity of the vaccine.

Pre-haemodialysis and haemodialysis patients

The reactogenicity profile of Fendrix in a total of 82 pre-haemodialysis and haemodialysis patients was generally comparable to that seen in healthy subjects.

List of adverse reactions

Adverse reactions reported in a clinical trial following primary vaccination with Fendrix and considered as being related or possibly related to vaccination have been categorised by frequency.

Frequencies are reported as:

Very common: ($\geq 1/10$)

Common: ($\geq 1/100$ to $< 1/10$)

Uncommon: ($\geq 1/1,000$ to $< 1/100$)

Rare: ($\geq 1/10,000$ to $< 1/1,000$)

Very rare: ($< 1/10,000$)

Clinical trial data

Nervous system disorders:

Very common: headache

Gastrointestinal disorders:

Common: gastrointestinal disorder

General disorders and administration site conditions:

Very common: fatigue, pain

Common: fever, injection site swelling, redness

Unsolicited symptoms considered to be at least possibly related to vaccination were uncommonly reported and consisted of rigors, other injection site reaction and maculo-papular rash.

Healthy subjects

The reactogenicity profile of Fendrix in healthy subjects was generally comparable to that seen in pre-haemodialysis and haemodialysis patients.

In a large double-blind randomised comparative study, healthy subjects were enrolled to receive a three dose primary course of Fendrix (N= 713) or a commercially available hepatitis B vaccine (N= 238) at 0, 1, 2 months. The most common adverse reactions reported were local reactions at the injection site.

Vaccination with Fendrix induced more transient local symptoms as compared to the comparator vaccine, with pain at the injection site being the most frequently reported solicited local symptom. However, solicited general symptoms were observed with similar frequencies in both groups.

Adverse reactions reported in a clinical trial following primary vaccination with Fendrix and considered as being at least possibly related to vaccination have been categorised by frequency.

Nervous system disorders:

Common: headache

Ear and labyrinth disorders:

Rare: vertigo

Gastrointestinal disorders:

Common: gastrointestinal disorder

Muskuloskeletal and connective tissue disorders:

Rare: tendinitis, back pain

Infections and infestations:

Rare: viral infection

General disorders and administration site conditions:

Very common: injection site swelling, fatigue, pain, redness

Common: fever

Uncommon: other injection site reaction

Rare: rigors, hot flushes, thirst, asthenia

Immune system disorders:

Rare: allergy

Psychiatric disorders:

Rare: nervousness

No increase in the incidence or severity of these adverse reactions was seen with subsequent doses of the primary vaccination schedule.

No increase in the reactogenicity was observed after the booster vaccination with respect to the primary vaccination.

- Experience with hepatitis B vaccine:

Following widespread use of hepatitis B vaccines, in very rare cases, syncope, paralysis, neuropathy, neuritis (including Guillain-Barré syndrome, optic neuritis and multiple sclerosis), encephalitis, encephalopathy, meningitis and convulsions have been reported. The causal relationship to the vaccine has not been established.

Anaphylaxis, allergic reactions including anaphylactoid reactions and mimicking serum sickness have also been reported very rarely with hepatitis B vaccines.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via (please see details below)

Ireland

HPRA Pharmacovigilance

Website: www.hpra.ie

4.9 Overdose

Limited data on overdose are available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, hepatitis vaccines, ATC code J07BC01.

Fendrix induces specific humoral antibodies against HBsAg (anti-HBs antibodies). An anti-HBs antibody titre ≥ 10 mIU/ml correlates with protection to HBV infection.

It can be expected that hepatitis D will also be prevented by immunisation with Fendrix as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

Immunological data

In pre-haemodialysis and haemodialysis patients:

In a comparative clinical study in 165 pre-haemodialysis and haemodialysis patients (15 years and above), protective levels of specific humoral antibodies (anti-HBs titres ≥ 10 mIU/ml) were observed in 74.4% of Fendrix recipients (N = 82) one month after the third dose (i.e at month 3), as compared to 52.4% of patients in the control group who received a double dose of a commercially available hepatitis B vaccine (N = 83) for this population.

At month 3, Geometric Mean Titres (GMT) were 223.0 mIU/ml and 50.1 mIU/ml in the Fendrix and control groups respectively, with 41.0% and 15.9% of subjects with anti-HBs antibody titres ≥ 100 mIU/ml respectively.

After completion of a four dose primary course (i.e at month 7), 90.9% of Fendrix recipients were seroprotected (≥ 10 mIU/ml) against hepatitis B, in comparison with 84.4% in a control group who received the commercially available hepatitis B vaccine.

At month 7, GMTs were 3559.2 mIU/ml and 933.0 mIU/ml in the Fendrix and control groups who received the commercially available hepatitis B vaccine respectively, with 83.1% and 67.5% of subjects with anti-HBs antibody titres ≥ 100 mIU/ml respectively.

Antibody persistence

In pre-haemodialysis and haemodialysis patients:

Anti-HBs antibodies have been shown to persist for at least 36 months following a 0, 1, 2, 6 month primary course of Fendrix in pre-haemodialysis and haemodialysis patients. At month 36, 80.4% of these patients retained protective antibody levels (anti-HBs titres ≥ 10 mIU/ml), as compared to 51.3% of patients who received a commercially available hepatitis B vaccine.

At month 36, GMTs were 154.1 mIU/ml and 111.9 mIU/ml in the Fendrix and control groups respectively, with 58.7% and 38.5% of subjects with anti-HBs antibody titres ≥ 100 mIU/ml respectively.

5.2 Pharmacokinetic properties

Pharmacokinetic properties of Fendrix or MPL alone has not been studied in humans.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional animal studies consisting of acute and repeated dose toxicity, cardiovascular and respiratory safety pharmacology and reproductive toxicity including pregnancy and peri and postnatal development of the pups till weaning (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

For adjuvants, see section 2.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Do not freeze.

Store in the original package in order to protect from light.

6.5 Nature and contents of container

0.5 ml of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and with a rubber tip cap.

The tip cap and rubber plunger stopper of the pre-filled syringe are made with synthetic rubber.

Pack sizes of 1 and 10, with or without needles.

Not all pack sizes may be marketed.

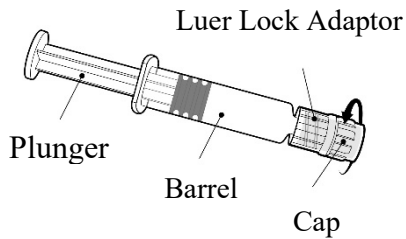
6.6 Special precautions for disposal and other handling

Upon storage, a fine white deposit with a clear colourless supernatant can be observed.

Before administration, the vaccine should be well shaken to obtain a slightly opaque, white suspension.

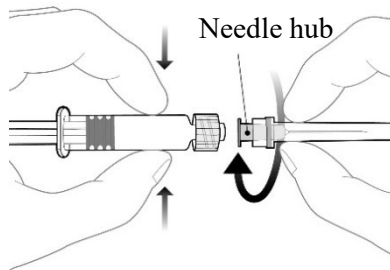
The vaccine should be visually inspected both before and after re-suspension for any foreign particulate matter and/or change in physical appearance. The vaccine must not be used if any change in the appearance of the vaccine has taken place.

Instructions for the pre-filled syringe



Hold the syringe by the barrel, not by the plunger.

Unscrew the syringe cap by twisting it anticlockwise.



To attach the needle, connect the hub to the Luer Lock Adaptor and rotate a quarter turn clockwise until you feel it lock.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/0299/001
EU/1/04/0299/002
EU/1/04/0299/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02 February 2005
Date of latest renewal: 17 November 2014

10. DATE OF REVISION OF THE TEXT

09/07/2026

Detailed information on this product is available on the website of the European Medicines Agency
<http://www.ema.europa.eu>