ANNEX I

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

[1]adjuvanted by AS04C containing:

- 3-*O*-desacyl-4'- monophosphoryl lipid A (MPL) [2]	50 micrograms

[2]adsorbed on aluminium phosphate (0.5 milligrams Al^{3+} in total)

[3]produced 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: (≥1/10)
Common: (≥1/100 to <1/10)
Uncommon: (≥1/1,000 to <1/100)
Rare: (≥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 the national reporting system listed in Appendix V.

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 ≥ 10mIU/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.

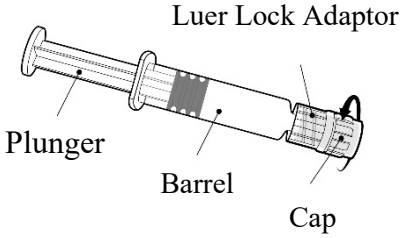
6.6 Special precautions for disposal and other handling

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.

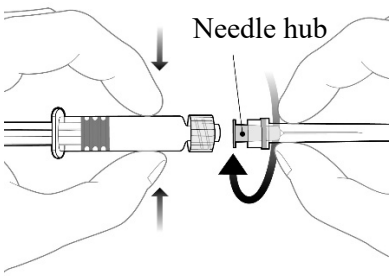
The vaccine should be visually inspected both before and after re-suspension for any foreign particulate matter and/or change in physical appearance. The vaccine must not be used if any change in the appearance of the vaccine has taken place.

<u>Instructions for the pre-filled syringe</u>



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

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

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

GlaxoSmithKline Biologicals S.A.
89, rue de l'Institut – 1330 Rixensart
Belgium

Name and address of the manufacturer responsible for batch release

GlaxoSmithKline Biologicals S.A.
89, rue de l'Institut – 1330 Rixensart
Belgium

B CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSUR)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

1 PRE-FILLED SYRINGE WITH SEPARATE NEEDLE
1 PRE-FILLED SYRINGE WITHOUT NEEDLE
10 PRE-FILLED SYRINGES WITHOUT NEEDLES

1. NAME OF THE MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml):
Hepatitis B surface antigen[1, 2, 3] 20 micrograms

[1]adjuvanted by AS04C containing:
- 3-*O*-desacyl-4'- monophosphoryl lipid A (MPL) [2] 50 micrograms

[2]adsorbed on aluminium phosphate (0.5 milligrams Al^{3+} in total)

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

3. LIST OF EXCIPIENTS

Sodium chloride
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

1 pre-filled syringe
1 separate needle
1 dose (0.5 ml)

1 pre-filled syringe
1 dose (0.5 ml)

10 pre-filled syringes
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Shake well before use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/0299/001 – pack of 1 with separate needle
EU/1/04/0299/002 – pack of 1 without needle
EU/1/04/0299/003 – pack of 10 without needles

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PREFILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Fendrix suspension for injection
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

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

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for you only. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Fendrix is and what it is used for
2. What you need to know before you receive Fendrix
3. How Fendrix is given
4. Possible side effects
5. How to store Fendrix
6. Contents of the pack and other information

1. What Fendrix is and what it is used for

Fendrix is a vaccine which prevents hepatitis B.
It is used for patients with kidney problems:
- patients having "haemo-dialysis"- where a "dialysis" machine removes waste products from the blood
- patients who are going to have "haemo-dialysis" in the future.

Fendrix is for adults and young people aged 15 years and above.

What is hepatitis B?

Hepatitis B is caused by a virus which makes the liver swollen.
- Signs may not be seen for 6 weeks to 6 months after infection.
- The main signs of the illness include mild signs of flu such as headache or fever, feeling very tired, dark urine, pale stools (faeces), yellow skin or eyes (jaundice). These or other signs may mean the person might need treatment in hospital. Most people fully recover from the illness.
- Some people with hepatitis B do not look or feel ill - they do not have any signs of illness.
- The virus is found in body fluids such as in the vagina, blood, semen, or saliva (spit).

Carriers of hepatitis B

- The hepatitis B virus stays in the body of some people all through their lives.
- This means they can still infect other people and are known as virus "carriers".
- Carriers of the virus are likely to get serious liver problems, such as "cirrhosis" or liver cancer.

How Fendrix works

- Fendrix helps your body to produce its own protection against the virus (antibodies). These antibodies will protect you against the disease.
- Fendrix contains two things called "MPL" (a non-toxic purified fat derivative from bacteria) and "aluminium phosphate". These make the vaccine work quicker, better and last for longer.
- As with all vaccines, a course of Fendrix cannot fully protect all people that are vaccinated.

- Fendrix may not protect you from being ill if you have already caught the hepatitis B virus.
- Fendrix can only help to protect you against infection with the hepatitis B virus. It cannot protect you against other infections that can affect the liver - even though these infections might have signs similar to those caused by the hepatitis B virus.

2. What you need to know before you receive Fendrix

Fendrix should not be given

- if you are allergic to the active substance, or any of the other ingredients of this vaccine (listed in section 6). Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue
- if you have ever had an allergic reaction to any vaccine against hepatitis B
- if you have a severe infection with a high temperature. The vaccine can be given after you have recovered. A minor infection such as a cold should not be a problem, but talk to your doctor first.

Fendrix should not be given if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before having Fendrix.

Warnings and precautions

Talk to your doctor or pharmacist before you are given Fendrix:

- if you have any known allergies
- if you have had any health problems after having a vaccine in the past.

Fainting can occur (mostly in adolescents) following, or even before, any needle injection. Therefore tell the doctor or nurse if you fainted with a previous injection.

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before having Fendrix.

Other medicines and Fendrix

Tell your doctor if you are taking, have recently taken, might take any other medicines or have recently received any other vaccine.

- You should have a gap of at least 2 to 3 weeks between having Fendrix and any other vaccine.
- Fendrix may need to be given at the same time as an injection of hepatitis B “immuno-globulins”. Your doctor will make sure that the vaccines are injected into different parts of the body.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think that you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this vaccine.

Driving and using machines

You may feel tired or get a headache after receiving Fendrix. If this happens, take special care while driving or using any tools or machines.

Fendrix contains sodium

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

3. How Fendrix is given

How the vaccine is given
The doctor or nurse will give Fendrix as an injection into your muscle. This is usually in your upper arm.

How much is given
- You will have a series of four injections.
- The injections will be given within 6 months:
  - First injection - on a date agreed with your doctor.
  - Second injection - 1 month after the first injection.
  - Third injection - 2 months after the first injection.
  - Fourth injection - 6 months after the first injection.

- The doctor or nurse will tell you when you should come back for the next injections.

- Once you have had the first injection of Fendrix, the next injections need also to be Fendrix (not another sort of hepatitis B vaccine).

Your doctor will tell you if you need any extra or "booster" injections in the future. Fendrix can also be used as a booster after a course of a different type of hepatitis B vaccine.

If you miss a dose

- **If you miss an injection, talk to your doctor and arrange another visit.**
- Make sure you finish the complete course of four injections. If not, you may not be fully protected against the disease.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

The following side effects may happen with this vaccine. Their frequency is defined using the conventions listed below:

Very common (these may occur with more than 1 in 10 doses of the vaccine): headache, feeling tired, pain or discomfort where the injection was given.

Common (these may occur with up to 1 in 10 doses of the vaccine): redness or swelling where the injection was given, fever, stomach and digestion problems.

Uncommon (these may occur with up to 1 in 100 doses of the vaccine**):** chills, red, raised skin rash, other reactions where the injection was given.

Rare (these may occur with up to 1 in 1,000 doses of the vaccine): allergy, hot flushes, feeling dizzy, feeling thirsty, feeling nervous, infection caused by a virus, back pain, swelling of your tendons.

Additionally, the following side effects have also been reported with other hepatitis B vaccines:

Very rare (these may occur with up to 1 in 10,000 doses of the vaccine): fits, fainting, problems with the nerves of your eye (optic neuritis), multiple sclerosis, loss of feeling or problems moving some parts of your body, severe headache with a stiff neck, numbness or weakness of the arms and legs (neuropathy), inflammation of nerves (neuritis), weakness and paralysis in the extremities and often

progressing to the chest and face (Guillain-Barré syndrome), swelling or infection of the brain (encephalitis, encephalopathy).
Allergic reactions, including anaphylactoid reactions, may also occur very rarely (with up to 1 in 10,000 doses of the vaccine). These may be local or widespread rashes that may be itchy or blistering, swelling of the eyes and face, difficulty in breathing or swallowing, a sudden drop in blood pressure and loss of consciousness. Such reactions may occur before leaving the doctor's surgery. However, you should seek immediate treatment in any event.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fendrix

- Keep this vaccine out of the sight and reach of children.

- Do not use this vaccine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

- Store in a refrigerator (2°C - 8°C).
- Store in the original package in order to protect from light.
- Do not freeze. Freezing destroys the vaccine.

- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Fendrix contains

- The active substance in 1 dose (0.5 ml) of Fendrix is:

Hepatitis B surface antigen [1, 2, 3] 20 micrograms

[1]adjuvanted by AS04C containing:
- 3-*O*-desacyl-4'- monophosphoryl lipid A (MPL) [2] 50 micrograms

[2]adsorbed on aluminium phosphate (0.5 milligrams Al^{3+} in total)

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

- The other ingredients in Fendrix are: sodium chloride, water for injections.

What Fendrix looks like and contents of the pack

Fendrix is a white and milky suspension.

Fendrix is available in 1-dose pre-filled syringe with or without separate needles, pack sizes of 1 and 10.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

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

For any information about this medicine, please contact the local representative of the Marketing Authorisation holder.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:

The following information is intended for healthcare professionals only:

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.

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

Fendrix should not be given to subjects with hypersensitivity to the active substance or to any of the excipients.

Fendrix should not be given to subjects with hypersensitivity after previous administration of other hepatitis B vaccines.

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

Fendrix should be injected intramuscularly in the deltoid region.

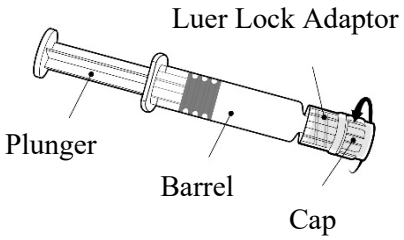
Since intramuscular administration into the gluteal muscle could lead to a suboptimal response to the vaccine, this route should be avoided.

Fendrix should under no circumstances be administered intradermally or intravenously.

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.

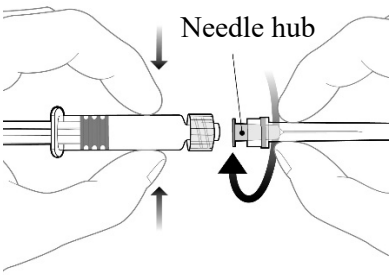
Appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

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