ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection

Hepatitis B vaccine (rDNA)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced in *Saccharomyces cerevisiae* (strain 2150-2-3) yeast by recombinant DNA technology

This vaccine may contain traces of formaldehyde and potassium thiocyanate, which are used during the manufacturing process. See sections 4.3, 4.4 and 4.8.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection
Slightly opaque white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HBVAXPRO is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals from birth through 15 years of age considered at risk of exposure to hepatitis B virus.

The specific at risk categories to be immunised are to be determined on the basis of the official recommendations.

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

4.2 Posology and method of administration

Posology
Individuals from birth through 15 years of age: 1 dose (0.5 ml)at each injection.

Primary vaccination:

A course of vaccination should include at least three injections.

Two primary immunisation schedules can be recommended:

0, 1, 6 months: two injections with an interval of one month; a third injection 6 months after the first administration.

0, 1, 2, 12 months: three injections with an interval of one month; a fourth dose should be administered at 12 months.

It is recommended that the vaccine be administered in the schedules indicated. Infants receiving the compressed regimen (0, 1, 2 months dosing schedule) must receive the 12 month booster to induce higher antibody titres.

Booster:

Immunocompetent vaccinees

The need for a booster dose in healthy individuals who have received a full primary vaccination course has not been established. However, some local vaccination schedules currently include a recommendation for a booster dose and these should be respected.

Immunocompromised vaccinees (e.g. dialysis patients, transplant patients, AIDS Patients)

In vaccinees with an impaired immune system, administration of additional doses of vaccine should be considered if the antibody level against hepatitis B virus surface antigen (anti-HBsAg) is less than 10 IU/l.

Revaccination of nonresponders

When persons who do not respond to the primary vaccine series are revaccinated, 15-25 % produce an adequate antibody response after one additional dose and 30-50 % after three additional doses. However, because data are insufficient concerning the safety of hepatitis B vaccine when additional doses in excess of the recommended series are administered, revaccination following completion of the primary series is not routinely recommended. Revaccination should be considered for high-risk individuals, after weighing the benefits of vaccination against the potential risk of experiencing increased local or systemic adverse reactions.

Special dosage recommendations:

Dosage recommendation for neonates of mothers who are hepatitis B virus carriers

- At birth, one dose of hepatitis B immunoglobulin (within 24 hours).
- The first dose of the vaccine should be given within 7 days of birth and can be administered simultaneously with hepatitis B immunoglobulin but at a separate injection site.
- Subsequent doses of vaccine should be given according to the locally recommended vaccination schedule.

Dosage recommendation for known or presumed exposure to hepatitis B virus (e.g needlestick with contaminated needle)

- Hepatitis B immunoglobulin should be given as soon as possible after exposure (within 24 hours).
- The first dose of the vaccine should be given within 7 days of exposure and can be administered simultaneously with hepatitis B immunoglobulin but at a separate injection site.
- Serologic testing is also recommended, with the administration of subsequent doses of vaccine, if necessary, (i.e according to the serologic status of the patient) for short and long term protection.

- In the case of unvaccinated or incompletely vaccinated individuals, additional doses should be given as in the recommended immunisation schedule. The accelerated schedule including the 12 month booster dose can be proposed.

Method of administration

This vaccine should be administered intramuscularly.

The anterolateral thigh is the preferred site for injection in neonates and infants. The deltoid muscle is the preferred site for injection in children and adolescents.

Do not inject intravascularly.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia or bleeding disorders.

Precautions to be taken before handling or administering the product: see section 6.6.

For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- History of hypersensitivity to the active substance, or to any of the excipients, or trace residuals (e.g. formaldehyde and potassium thiocyanate) (see sections 6.1 and 2)
- Vaccination should be postponed in individuals with a severe febrile illness or acute infection.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

This vaccine may contain traces of formaldehyde and potassium thiocyanate, which are used during the manufacturing process. Therefore, hypersensitivity reactions may occur (see sections 2 and 4.8).

For clinical or laboratory monitoring regarding immunocompromised individuals or individuals with known or presumed exposure to hepatitis B virus, see section 4.2

The potential risk of apnoea and the need for respiratory monitoring for 48 to 72 hours should be considered when administering the primary immunisation series to very premature infants (born $\leq$ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity (see section 4.8). As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Because of the long incubation period of hepatitis B, it is possible for unrecognised hepatitis B infection to be present at the time of vaccination. 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 and other pathogens known to infect the liver.

Caution should be exercised when prescribing to pregnant or breastfeeding women. (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

This vaccine can be administered:
- with hepatitis B immunoglobulin, at a separate injection site.
- to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
- concomitantly with other vaccines, using separate sites and syringes.

The concomitant administration of pneumococcal conjugate vaccine (PREVENAR) given with hepatitis B vaccine using the 0, 1 and 6 and 0, 1, 2 and 12 month schedules has not been sufficiently studied.

4.6 Fertility, pregnancy and lactation

Fertility:
HBVAXPRO has not been evaluated in fertility studies.

Pregnancy:
There is no clinical data on the use of HBVAXPRO on pregnant women.

The vaccine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breastfeeding:
There is no clinical data on the use of HBVAXPRO on breastfeeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most common side effects seen are injection-site reactions: transient soreness, erythema, induration.

b. Tabulated summary of adverse reactions

The following undesirable effects have been reported following the widespread use of the vaccine.
As with other hepatitis B vaccines, in many instances, the causal relationship to the vaccine has not been established.

Adverse reactions	Frequency
General disorders and administration site conditions	
Local reactions (injection site): Transient soreness, Erythema, Induration	Common (≥1/100 to, <1/10)
Fatigue, Fever, Malaise, Influenza-like symptoms	Very rare (<1/10,000)
Blood and the lymphatic system disorders	
Thrombocytopenia, Lymphadenopathy	Very rare (<1/10,000)
Immune system disorders	
Serum sickness, Anaphylaxis, Polyarteritis nodosa	Very rare (<1/10,000)
Nervous system disorders	

Paresthesia, Paralysis (including Bell's palsy, facial paralysis), Peripheral neuropathies (polyradiculoneuritis, Guillain Barre Syndrome), Neuritis (including optical neuritis), Myelitis (including transverse Myelitis), Encephalitis, Demyelinating disease of the central nervous system, Exacerbation of multiple sclerosis, Multiple sclerosis, Seizure, Headache, Dizziness, Syncope	Very rare (<1/10,000)
Vascular disorders	
Hypotension, Vasculitis	Very rare (<1/10,000)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm-like symptoms	Very rare (<1/10,000)
Gastrointestinal disorders	
Vomiting, Nausea, Diarrhoea, Abdominal pain	Very rare (<1/10,000)
Skin and subcutaneous tissue disorders	
Rash, Alopecia, Pruritus, Urticaria, Erythema multiforme, Angioedema, Eczema	Very rare (<1/10,000)
Musculoskeletal, connective tissue and bone disorders	
Arthralgia, Arthritis, Myalgia, Pain in extremity	Very rare (<1/10,000)
Investigations	
Elevation of liver enzymes	Very rare (<1/10,000)

c. Other special population
Apnoea in very premature infants (born ≤ 28 weeks of gestation) (see section 4.4)

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectious, ATC code: J07BC01

The vaccine induces specific humoral antibodies against hepatitis B virus surface antigen (anti-HBsAg). Development of an antibody titre against hepatitis B virus surface antigen (anti-HBsAg) equal to or greater than 10 IU/l measured 1 to 2 months after the last injection correlates with protection to hepatitis B virus infection.

In clinical trials, 96 % of 1,497 healthy infants, children, adolescents and adults given a 3 dose course of a previous formulation of Merck's recombinant hepatitis B vaccine developed a protective level of antibodies against hepatitis B virus surface antigen (≥ 10 IU/l). In two infant trials using different dosing schedules and concomitant vaccines, the proportion of infants with protective levels of antibodies were 97.5 % and 97.2 % with geometric mean titres of 214 and 297 IU/l, respectively.

The protective efficacy of a dose of hepatitis B immunoglobulin at birth followed by 3 doses of a previous formulation of Merck's recombinant hepatitis B vaccine has been demonstrated for neonates born to mothers positive for both hepatitis B virus surface antigen (HBsAg) and hepatitis B virus e antigen (HBeAg). Among 130 vaccinated infants, the estimated efficacy in prevention of chronic hepatitis B infection was 95 % as compared to the infection rate in untreated historical controls.

Although the duration of the protective effect of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy vaccinees is unknown, follow-up over 5-9 years of approximately 3,000 high-risk

subjects given a similar plasma-derived vaccine has revealed no cases of clinically apparent hepatitis B infection.

In addition, persistence of vaccine-induced immunologic memory for hepatitis B virus surface antigen (HBsAg) has been demonstrated through an anamnestic antibody response to a booster dose of a previous formulation of Merck's recombinant hepatitis B vaccine. As with other hepatitis B vaccines, the duration of the protective effect in healthy vaccinees is unknown at present. The need for a booster dose of HBVAXPRO is not yet defined beyond the 12 month booster dose required for the 0, 1, 2 compressed schedule.

Reduced risk of Hepatocellular Carcinoma
Hepatocellular carcinoma is a serious complication of hepatitis B virus infection. Studies have demonstrated the link between chronic hepatitis B infection and hepatocellular carcinoma and 80 % of hepatocellular carcinomas are caused by hepatitis B virus infection. Hepatitis B vaccine has been recognized as the first anti-cancer vaccine because it can prevent primary liver cancer.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Animal reproduction studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Borax
Water for injections

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.

6.5 Nature and contents of container

0.5 ml of suspension in vial (glass) with stopper (gray butyl rubber) and aluminum seals with plastic flip caps. Pack size of 1, 10.

0.5 ml of suspension in vial (glass) with stopper (gray butyl rubber) and aluminum seals with plastic flip caps with an empty sterile injection syringe with needle. Pack size of 1.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be inspected visually in order to detect any appearance of precipitate or discolouring of the content prior to administration. If these conditions exist, the product should not be administered.
Before use, the vial should be well shaken.
Once the vial has been penetrated, the withdrawn vaccine should be used promptly, and the vial must be discarded.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/001
EU/1/01/183/018
EU/1/01/183/019

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27/04/2001
Date of latest renewal: 04/08/2006

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

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection in pre-filled syringe

Hepatitis B vaccine (rDNA)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced in *Saccharomyces cerevisiae* (strain 2150-2-3) yeast by recombinant DNA technology.

This vaccine may contain traces of formaldehyde and potassium thiocyanate, which are used during the manufacturing process. See section 4.3, 4.4 and 4.8.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe
Slightly opaque white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HBVAXPRO is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals from birth through 15 years of age considered at risk of exposure to hepatitis B virus.

The specific at risk categories to be immunised are to be determined on the basis of the official recommendations.

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

4.2 Posology and method of administration

Posology
Individuals from birth through 15 years of age: 1 dose (0.5 ml) at each injection.

Primary vaccination:

A course of vaccination should include at least three injections.

Two primary immunisation schedules can be recommended:

0, 1, 6 months: two injections with an interval of one month; a third injection 6 months after the first administration.

0, 1, 2, 12 months: three injections with an interval of one month; a fourth dose should be administered at 12 months.

It is recommended that the vaccine be administered in the schedules indicated. Infants receiving the compressed regimen (0, 1, 2 months dosing schedule) must receive the 12 month booster to induce higher antibody titres.

Booster:

Immunocompetent vaccinees

The need for a booster dose in healthy individuals who have received a full primary vaccination course has not been established. However, some local vaccination schedules currently include a recommendation for a booster dose and these should be respected.

Immunocompromised vaccinees (e.g. dialysis patients, transplant patients, AIDS Patients)

In vaccinees with an impaired immune system, administration of additional doses of vaccine should be considered if the antibody level against hepatitis B virus surface antigen (anti-HBsAg) is less than 10 IU/l.

Revaccination of nonresponders

When persons who do not respond to the primary vaccine series are revaccinated, 15-25 % produce an adequate antibody response after one additional dose and 30-50 % after three additional doses. However, because data are insufficient concerning the safety of hepatitis B vaccine when additional doses in excess of the recommended series are administered, revaccination following completion of the primary series is not routinely recommended. Revaccination should be considered for high-risk individuals, after weighing the benefits of vaccination against the potential risk of experiencing increased local or systemic adverse reactions.

Special dosage recommendations:

Dosage recommendations for neonates born to mothers who are hepatitis B virus carriers

- At birth, one dose of hepatitis B immunoglobulin (within 24 hours).
- The first dose of the vaccine should be given within 7 days of birth and can be administered simultaneously with hepatitis B immunoglobulin at birth, but at a separate injection site.
- Subsequent doses of vaccine should be given according to the locally recommended vaccination schedule.

Dosage recommendation for known or presumed exposure to hepatitis B virus (e.g needlestick with contaminated needle)

- Hepatitis B immunoglobulin should be given as soon as possible after exposure (within 24 hours).
- The first dose of the vaccine should be given within 7 days of exposure and can be administered simultaneously with hepatitis B immunoglobulin but at a separate injection site.
- Serologic testing is also recommended, with the administration of subsequent doses of vaccine, if necessary, (i.e according to the serologic status of the patient) for short and long term protection.

- In the case of unvaccinated or incompletely vaccinated individuals, additional doses should be given as in the recommended immunisation schedule. The accelerated schedule including the 12 month booster dose can be proposed.

Method of administration

This vaccine should be administered intramuscularly.

The anterolateral thigh is the preferred site for injection in neonates and infants. The deltoid muscle is the preferred site for injection in children and adolescents.

Do not inject intravascularly.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia or bleeding disorders.

Precautions to be taken before handling or administering the product: see section 6.6.

For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- History of hypersensitivity to the active substance, or to any of the excipients, or trace residuals (e.g. formaldehyde and potassium thiocyanate) (see sections 6.1 and 2)
- Vaccination should be postponed in individuals with a severe febrile illness or acute infection.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

This vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. Therefore, hypersensitivity reactions may occur (see sections 2 and 4.8).

For clinical or laboratory monitoring regarding immunocompromised individuals or individuals with known or presumed exposure to hepatitis B virus, see section 4.2.

The potential risk of apnoea and the need for respiratory monitoring for 48 to 72 hours should be considered when administering the primary immunisation series to very premature infants (born $\leq$ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity (see section 4.8). As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Because of the long incubation period of hepatitis B, it is possible for unrecognised hepatitis B infection to be present at the time of vaccination. 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 and other pathogens known to infect the liver.

Caution should be exercised when prescribing to pregnant or breastfeeding women. (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

This vaccine can be administered:
- with hepatitis B immunoglobulin, at a separate injection site.
- to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
- concomitantly with other vaccines, using separate sites and syringes.

The concomitant administration of pneumococcal conjugate vaccine (PREVENAR) given with hepatitis B vaccine using the 0, 1 and 6 and 0, 1, 2 and 12 month schedules has not been sufficiently studied.

4.6 Fertility, pregnancy and lactation

Fertility:
HBVAXPRO has not been evaluated in fertility studies.

Pregnancy:
There is no clinical data on the use of HBVAXPRO on pregnant women.
The vaccine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breastfeeding:
There is no clinical data on the use of HBVAXPRO on breastfeeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most common side effects seen are injection-site reactions: transient soreness, erythema, induration.

b. Tabulated summary of adverse reactions

The following undesirable effects have been reported following the widespread use of the vaccine.

As with other hepatitis B vaccines, in many instances, the causal relationship to the vaccine has not been established.

Adverse reactions	Frequency
General disorders and administration site conditions	
Local reactions (injection site): Transient soreness, Erythema, Induration	Common (≥1/100 to, <1/10)
Fatigue, Fever, Malaise, Influenza-like symptoms	Very rare (<1/10,000)
Blood and the lymphatic system disorders	
Thrombocytopenia, Lymphadenopathy	Very rare (<1/10,000)
Immune system disorders	
Serum sickness, Anaphylaxis, Polyarteritis nodosa	Very rare (<1/10,000)
Nervous system disorders	

Paresthesia, Paralysis (including Bell's palsy, facial paralysis), Peripheral neuropathies (polyradiculoneuritis, Guillain Barre Syndrome), Neuritis (including optical neuritis), Myelitis (including transverse Myelitis), Encephalitis, Demyelinating disease of the central nervous system, Exacerbation of multiple sclerosis, Multiple sclerosis, Seizure, Headache, Dizziness, Syncope	Very rare (<1/10,000)
Vascular disorders	
Hypotension, Vasculitis	Very rare (<1/10,000)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm-like symptoms	Very rare (<1/10,000)
Gastrointestinal disorders	
Vomiting, Nausea, Diarrhoea, Abdominal pain	Very rare (<1/10,000)
Skin and subcutaneous tissue disorders	
Rash, Alopecia, Pruritus, Urticaria, Erythema multiforme, Angioedema, Eczema	Very rare (<1/10,000)
Musculoskeletal, connective tissue and bone disorders	
Arthralgia, Arthritis, Myalgia, Pain in extremity	Very rare (<1/10,000)
Investigations	
Elevation of liver enzymes	Very rare (<1/10,000)

c. Other special population
Apnoea in very premature infants (born ≤ 28 weeks of gestation) (see section 4.4)

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectious, ATC code: J07BC01

The vaccine induces specific humoral antibodies against hepatitis B virus surface antigen (anti-HBsAg). Development of an antibody titre against hepatitis B virus surface antigen (anti-HBsAg) equal to or greater than 10 IU/l measured 1 to 2 months after the last injection correlates with protection to hepatitis B virus infection.

In clinical trials, 96 % of 1,497 healthy infants, children, adolescents and adults given a 3 dose course of a previous formulation of Merck's recombinant hepatitis B vaccine developed a protective level of antibodies against hepatitis B virus surface antigen (≥ 10 IU/l). In two infant trials using different dosing schedules and concomitant vaccines, the proportion of infants with protective levels of antibodies were 97.5 % and 97.2 % with geometric mean titres of 214 and 297 IU/l, respectively.

The protective efficacy of a dose of hepatitis B immunoglobulin at birth followed by 3 doses of a previous formulation of Merck's recombinant hepatitis B vaccine has been demonstrated for neonates born to mothers positive for both hepatitis B virus surface antigen (HBsAg) and hepatitis B virus e antigen (HBeAg). Among 130 vaccinated infants, the estimated efficacy in prevention of chronic hepatitis B infection was 95 % as compared to the infection rate in untreated historical controls.

Although the duration of the protective effect of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy vaccinees is unknown, follow-up over 5-9 years of approximately 3,000 high-risk subjects given a similar plasma-derived vaccine has revealed no cases of clinically apparent hepatitis B infection.

In addition, persistence of vaccine-induced immunologic memory for hepatitis B virus surface antigen (HBsAg) has been demonstrated through an anamnestic antibody response to a booster dose of a previous formulation of Merck's recombinant hepatitis B vaccine. As with other hepatitis B vaccines, the duration of the protective effect in healthy vaccinees is unknown at present. The need for a booster dose of HBVAXPRO is not yet defined beyond the 12 month booster dose required for the 0, 1, 2 compressed schedule.

Reduced risk of Hepatocellular Carcinoma
Hepatocellular carcinoma is a serious complication of hepatitis B virus infection. Studies have demonstrated the link between chronic hepatitis B infection and hepatocellular carcinoma and 80 % of hepatocellular carcinomas are caused by hepatitis B virus infection. Hepatitis B vaccine has been recognized as the first anti-cancer vaccine because it can prevent primary liver cancer.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Animal reproduction studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Borax
Water for injections

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.

6.5 Nature and contents of container

0.5 ml of suspension in pre-filled syringe (glass) without needle with a plunger stopper (gray chlorobutyl). Pack size of 1, 10, 20, 50.

0.5 ml of suspension in pre-filled syringe (glass) with 1 separate needle with a plunger stopper (gray chlorobutyl). Pack size of 1, 10.
0.5 ml of suspension in pre-filled syringe (glass) with 2 separate needles with a plunger stopper (gray chlorobutyl). Pack size of 1, 10, 20, 50.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be inspected visually in order to detect any appearance of precipitate or discolouring of the content prior to administration. If these conditions exist, the product should not be administered.
Before use, the syringe should be well shaken.
Hold the syringe barrel and attach the needle by twisting in clockwise direction, until the needle fits securely on the syringe.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/004
EU/1/01/183/005
EU/1/01/183/020
EU/1/01/183/021
EU/1/01/183/022
EU/1/01/183/023
EU/1/01/183/024
EU/1/01/183/025
EU/1/01/183/030
EU/1/01/183/031

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27/04/2001
Date of latest renewal: 04/08/2006

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

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 10 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced in *Saccharomyces cerevisiae* (strain 2150-2-3) yeast by recombinant DNA technology.

The vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. See sections 4.3, 4.4 and 4.8.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection
Slightly opaque white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HBVAXPRO is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals 16 years of age or more considered at risk of exposure to hepatitis B virus.

The specific at risk categories to be immunised are to be determined on the basis of the official recommendations.

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

4.2 Posology and method of administration

Posology
Individuals 16 years of age or more: 1 dose (1 ml) at each injection.

Primary vaccination:

A course of vaccination should include at least three injections.

Two primary immunisation schedules can be recommended:

0, 1, 6 months: two injections with an interval of one month; a third injection 6 months after the first administration.

0, 1, 2, 12 months: three injections with an interval of one month; a fourth dose should be administered at 12 months.

It is recommended that the vaccine be administered in the schedules indicated. Those receiving the compressed regimen (0, 1, 2 months dosing schedule) must receive the 12 month booster to induce higher antibody titres.

Booster:

Immunocompetent vaccinees

The need for a booster dose in healthy individuals who have received a full primary vaccination course has not been established. However, some local vaccination schedules currently include a recommendation for a booster dose and these should be respected.

Immunocompromised vaccinees (e.g. dialysis patients, transplant patients, AIDS Patients)

In vaccinees with an impaired immune system, administration of additional doses of vaccine should be considered if the antibody level against hepatitis B virus surface antigen (anti-HBsAg) is less than 10 IU/l.

Revaccination of nonresponders

When persons who do not respond to the primary vaccine series are revaccinated, 15-25 % produce an adequate antibody response after one additional dose and 30-50 % after three additional doses. However, because data are insufficient concerning the safety of hepatitis B vaccine when additional doses in excess of the recommended series are administered, revaccination following completion of the primary series is not routinely recommended. Revaccination should be considered for high-risk individuals, after weighing the benefits of vaccination against the potential risk of experiencing increased local or systemic adverse reactions.

Special dosage recommendations for known or presumed exposure to hepatitis B virus (e.g needlestick with contaminated needle):

- Hepatitis B immunoglobulin should be given as soon as possible after exposure (within 24 hours).
- The first dose of the vaccine should be given within 7 days of exposure and can be administered simultaneously with hepatitis B immunoglobulin, but at a separate injection site.
- Serologic testing is also recommended, with the administration of subsequent doses of vaccine, if necessary, (i.e according to the serologic status of the patient) for short and long term protection.
- In the case of unvaccinated or incompletely vaccinated individuals, additional doses should be given as in the recommended immunisation schedule. The accelerated schedule including the 12 month booster dose can be proposed.

Posology in individuals less than 16 years of age
HBVAXPRO 10 micrograms is not indicated in this subset of paediatric population.

The appropriate strength for administration to individuals from birth through 15 years of age is HBVAXPRO 5 micrograms.

Method of administration

This vaccine should be administered intramuscularly.

The deltoid muscle is the preferred site for injection in adults and adolescents.

Do not inject intravascularly.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia or bleeding disorders.

Precautions to be taken before handling or administering the product: see section 6.6.

For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- History of hypersensitivity to the active substance, or to any of the excipients, or trace residuals (e.g. formaldehyde and potassium thiocyanate) (see sections 6.1 and 2)
- Vaccination should be postponed in individuals with a severe febrile illness or acute infection.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

This vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. Therefore, hypersensitivity reactions may occur (see sections 2 and 4.8).

For clinical or laboratory monitoring regarding immunocompromised individuals or individuals with known or presumed exposure to hepatitis B virus, see section 4.2.

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 HBVAXPRO. Additional doses may need to be considered for persons who do not respond or have a sub-optimal response to a course of vaccinations.

Because of the long incubation period of hepatitis B, it is possible for unrecognised hepatitis B infection to be present at the time of vaccination. 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 and other pathogens known to infect the liver.
Caution should be exercised when prescribing to pregnant or breastfeeding women. (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

This vaccine can be administered:
- with hepatitis B immunoglobulin, at a separate injection site.
- to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
- concomitantly with other vaccines, using separate sites and syringes.

4.6 Fertility, pregnancy and lactation

Fertility:

HBVAXPRO has not been evaluated in fertility studies.

Pregnancy:
There is no clinical data on the use of HBVAXPRO in pregnant women
The vaccine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breastfeeding:
There is no clinical data on the use of HBVAXPRO on breastfeeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most common side effects seen are injection-site reactions: transient soreness, erythema, induration.

b. Tabulated summary of adverse reactions

The following undesirable effects have been reported following the widespread use of the vaccine.

As with other hepatitis B vaccines, in many instances, the causal relationship to the vaccine has not been established.

Adverse reactions	Frequency
General disorders and administration site conditions	
Local reactions (injection site): Transient soreness, Erythema, Induration	Common (≥1/100 to, <1/10)
Fatigue, Fever, Malaise, Influenza-like symptoms	Very rare (<1/10,000)
Blood and the lymphatic system disorders	
Thrombocytopenia, Lymphadenopathy	Very rare (<1/10,000)
Immune system disorders	
Serum sickness, Anaphylaxis, Polyarteritis nodosa	Very rare (<1/10,000)
Nervous system disorders	
Paresthesia, Paralysis (including Bell's palsy, facial paralysis), Peripheral neuropathies (polyradiculoneuritis, Guillain Barre Syndrome), Neuritis (including optical neuritis), Myelitis (including transverse Myelitis), Encephalitis, Demyelinating disease of the central nervous system, Exacerbation of multiple sclerosis, Multiple sclerosis, Seizure, Headache, Dizziness, Syncope	Very rare (<1/10,000)
Vascular disorders	
Hypotension, Vasculitis	Very rare (<1/10,000)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm-like symptoms	Very rare (<1/10,000)
Gastrointestinal disorders	
Vomiting, Nausea, Diarrhoea, Abdominal pain	Very rare (<1/10,000)
Skin and subcutaneous tissue disorders	

Rash, Alopecia, Pruritus, Urticaria, Erythema multiforme, Angioedema, Eczema	Very rare (<1/10,000)
Musculoskeletal, connective tissue and bone disorders	
Arthralgia, Arthritis, Myalgia, Pain in extremity	Very rare (<1/10,000)
Investigations	
Elevation of liver enzymes	Very rare (<1/10,000)

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectious, ATC code: J07BC01

The vaccine induces specific humoral antibodies against hepatitis B virus surface antigen (anti-HBsAg). Development of an antibody titre against hepatitis B (anti-HBsAg) equal to or greater than 10 IU/l measured 1 to 2 months after the last injection correlates with protection to hepatitis B virus infection.

In clinical trials, 96 % of 1,497 healthy infants, children, adolescents and adults given a 3 dose course of a previous formulation of Merck's recombinant hepatitis B vaccine developed a protective level of antibodies against hepatitis B virus surface antigen (≥ 10 IU/l). In two trials conducted in older adolescents and adults, 95.6-97.5 % of vaccinees developed a protective level of antibodies, with geometric mean titres in these trials ranging from 535 – 793 IU/l.

Although the duration of the protective effect of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy vaccinees is unknown, follow-up over 5-9 years of approximately 3,000 high-risk subjects given a similar plasma-derived vaccine has revealed no cases of clinically apparent hepatitis B infection.

In addition, persistence of vaccine-induced immunologic memory for hepatitis B virus surface antigen (HBsAg) has been demonstrated through an anamnestic antibody response to a booster dose of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy adults. As with other hepatitis B vaccines, the duration of the protective effect in healthy vaccinees is unknown at present. The need for a booster dose of HBVAXPRO is not yet defined beyond the 12 month booster dose required for the 0, 1, 2 compressed schedule.

Reduced risk of Hepatocellular Carcinoma
Hepatocellular carcinoma is a serious complication of hepatitis B virus infection. Studies have demonstrated the link between chronic hepatitis B infection and hepatocellular carcinoma and 80 % of hepatocellular carcinomas are caused by hepatitis B virus infection. Hepatitis B vaccine has been recognized as the first anti-cancer vaccine because it can prevent primary liver cancer.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Animal reproduction studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Borax
Water for injections

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.

6.5 Nature and contents of container

1 ml of suspension in vial (glass) with stopper (gray butyl rubber) and aluminum seals with plastic flip caps. Pack size of 1, 10.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be inspected visually in order to detect any appearance of precipitate or discolouring of the content prior to administration. If these conditions exist, the product should not be administered.
Before use, the vial should be well shaken.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/007
EU/1/01/183/008

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27/04/2001
Date of latest renewal: 04/08/2006

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

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 10 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced in *Saccharomyces cerevisiae* (strain 2150-2-3) yeast by recombinant DNA technology.

The vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. See sections 4.3, 4.4 and 4.8.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe
Slightly opaque white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HBVAXPRO is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals 16 years of age or more considered at risk of exposure to hepatitis B virus.

The specific at risk categories to be immunised are to be determined on the basis of the official recommendations.

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

4.2 Posology and method of administration

Posology

Individuals 16 years of age or more: 1 dose (1 ml) at each injection.

Primary vaccination:

A course of vaccination should include at least three injections.

Two primary immunisation schedules can be recommended:

*0, 1, 6 month*s: two injections with an interval of one month; a third injection 6 months after the first administration.

*0, 1, 2, 12 month*s: three injections with an interval of one month; a fourth dose should be administered at 12 months.

It is recommended that the vaccine be administered in the schedules indicated. Those receiving the compressed regimen (0, 1, 2 months dosing schedule) must receive the 12 month booster to induce higher antibody titres.

Booster:

Immunocompetent vaccinees

The need for a booster dose in healthy individuals who have received a full primary vaccination course has not been established. However, some local vaccination schedules currently include a recommendation for a booster dose and these should be respected.

Immunocompromised vaccinees (e.g. dialysis patients, transplant patients, AIDS Patients)

In vaccinees with an impaired immune system, administration of additional doses of vaccine should be considered if the antibody level against hepatitis B virus surface antigen (anti-HBsAg) is less than 10 IU/l.

Revaccination of nonresponders

When persons who do not respond to the primary vaccine series are revaccinated, 15-25 % produce an adequate antibody response after one additional dose and 30-50 % after three additional doses. However, because data are insufficient concerning the safety of hepatitis B vaccine when additional doses in excess of the recommended series are administered, revaccination following completion of the primary series is not routinely recommended. Revaccination should be considered for high-risk individuals, after weighing the benefits of vaccination against the potential risk of experiencing increased local or systemic adverse reactions.

Special dosage recommendations for known or presumed exposure to hepatitis B virus (e.g needlestick with contaminated needle):

- Hepatitis B immunoglobulin should be given as soon as possible after exposure (within 24 hours).
- The first dose of the vaccine should be given within 7 days of exposure and can be administered simultaneously with hepatitis B immunoglobulin but at a separate injection site.
- Serologic testing is also recommended, with the administration of subsequent doses of vaccine, if necessary, (i.e according to the serologic status of the patient) for short and long term protection.
- In the case of unvaccinated or incompletely vaccinates individuals, additional doses should be given as in the recommended immunisation schedules. The accelerated schedule including the 12 month booster dose can be proposed.

Posology in individuals less than 16 years of age
HBVAXPRO 10 micrograms is not indicated in this subset of paediatric population.

The appropriate strength for administration to individuals from birth through 15 years of age is HBVAXPRO 5 micrograms.

Method of administration

This vaccine should be administered intramuscularly.

The deltoid muscle is the preferred site for injection in adults and adolescents.

Do not inject intravascularly.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia or bleeding disorders.

Precautions to be taken before handling or administering the product: see section 6.6.

For instructions on preparation of the medicinal product before administration, see section 6.6

4.3 Contraindications

- History of hypersensitivity to the active substance, or to any of the excipients, or trace residuals (e.g. formaldehyde and potassium thiocyanate) (see sections 6.1 and 2)
- Vaccination should be postponed in individuals with a severe febrile illness or acute infection.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

This vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. Therefore, hypersensitivity reactions may occur (see sections 2 and 4.8).

For clinical or laboratory monitoring regarding immunocompromised individuals or individuals with known or presumed exposure to hepatitis B virus, see section 4.2.

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 HBVAXPRO. Additional doses may need to be considered for persons who do not respond or have a sub-optimal response to a course of vaccinations.

Because of the long incubation period of hepatitis B, it is possible for unrecognised hepatitis B infection to be present at the time of vaccination. 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 and other pathogens known to infect the liver.

Caution should be exercised when prescribing to pregnant or breastfeeding women. (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

This vaccine can be administered:
- with hepatitis B immunoglobulin, at a separate injection site.
- to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
- concomitantly with other vaccines, using separate sites and syringes.

4.6 Fertility, pregnancy and lactation

Fertility:
HBVAXPRO has not been evaluated in fertility studies.

Pregnancy:
There is no clinical data on the use of HBVAXPRO on pregnant women.
The vaccine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breastfeeding:
There is no clinical data on the use of HBVAXPRO on breastfeeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most common side effects seen are injection-site reactions: transient soreness, erythema, induration.

b. Tabulated summary of adverse reactions

The following undesirable effects have been reported following the widespread use of the vaccine.

As with other hepatitis B vaccines, in many instances, the causal relationship to the vaccine has not been established.

Adverse reactions	Frequency
General disorders and administration site conditions	
Local reactions (injection site): Transient soreness, Erythema, Induration	Common (≥1/100 to, <1/10)
Fatigue, Fever, Malaise, Influenza-like symptoms	Very rare (<1/10,000)
Blood and the lymphatic system disorders	
Thrombocytopenia, Lymphadenopathy	Very rare (<1/10,000)
Immune system disorders	
Serum sickness, Anaphylaxis, Polyarteritis nodosa	Very rare (<1/10,000)
Nervous system disorders	
Paresthesia, Paralysis (including Bell's palsy, facial paralysis), Peripheral neuropathies (polyradiculoneuritis, Guillain Barre Syndrome), Neuritis (including optical neuritis), Myelitis (including transverse Myelitis), Encephalitis, Demyelinating disease of the central nervous system, Exacerbation of multiple sclerosis, Multiple sclerosis, Seizure, Headache, Dizziness, Syncope	Very rare (<1/10,000)
Vascular disorders	
Hypotension, Vasculitis	Very rare (<1/10,000)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm-like symptoms	Very rare (<1/10,000)
Gastrointestinal disorders	
Vomiting, Nausea, Diarrhoea, Abdominal pain	Very rare (<1/10,000)

Skin and subcutaneous tissue disorders	
Rash, Alopecia, Pruritus, Urticaria, Erythema multiforme, Angioedema, Eczema	Very rare (<1/10,000)
Musculoskeletal, connective tissue and bone disorders	
Arthralgia, Arthritis, Myalgia, Pain in extremity	Very rare (<1/10,000)
Investigations	
Elevation of liver enzymes	Very rare (<1/10,000)

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectious, ATC code: J07BC01

The vaccine induces specific humoral antibodies against hepatitis B virus surface antigen (anti-HBsAg). Development of an antibody titre against hepatitis B virus surface antigen (anti-HBsAg) equal to or greater than 10 IU/l measured 1 to 2 months after the last injection correlates with protection to hepatitis B virus infection.

In clinical trials, 96 % of 1,497 healthy infants, children, adolescents and adults given a 3 dose course of a previous formulation of Merck's recombinant hepatitis B vaccine developed a protective level of antibodies against hepatitis B virus surface antigen (≥ 10 IU/l). In two trials conducted in older adolescents and adults, 95.6-97.5 % of vaccinees developed a protective level of antibodies, with geometric mean titres in these trials ranging from 535 – 793 IU/l.

Although the duration of the protective effect of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy vaccinees is unknown, follow-up over 5-9 years of approximately 3,000 high-risk subjects given a similar plasma-derived vaccine has revealed no cases of clinically apparent hepatitis B infection.

In addition, persistence of vaccine-induced immunologic memory for hepatitis B virus surface antigen (HBsAg) has been demonstrated through an anamnestic antibody response to a booster dose of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy adults. As with other hepatitis B vaccines, the duration of the protective effect in healthy vaccinees is unknown at present. The need for a booster dose of HBVAXPRO is not yet defined beyond the 12 month booster dose required for the 0, 1, 2 compressed schedule.

Reduced risk of Hepatocellular Carcinoma
Hepatocellular carcinoma is a serious complication of hepatitis B virus infection. Studies have demonstrated the link between chronic hepatitis B infection and hepatocellular carcinoma and 80 % of hepatocellular carcinomas are caused by hepatitis B virus infection. Hepatitis B vaccine has been recognized as the first anti-cancer vaccine because it can prevent primary liver cancer.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Animal reproduction studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Borax
Water for injections

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.

6.5 Nature and contents of container

1 ml of suspension in pre-filled syringe (glass) without needle with a plunger stopper (gray chlorobutyl). Pack size of 1, 10
1 ml of suspension in pre-filled syringe (glass) with 1 separate needle with a plunger stopper (gray chlorobutyl). Pack size of 1, 10
1 ml of suspension in pre-filled syringe (glass) with 2 separate needles with a plunger stopper (gray chlorobutyl). Pack size of 1, 10, 20
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be inspected visually in order to detect any appearance of precipitate or discolouring of the content prior to administration. If these conditions exist, the product should not be administered.
Before use, the syringe should be well shaken.
Hold the syringe barrel and attach the needle by twisting in clockwise direction, until the needle fits securely on the syringe.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/011
EU/1/01/183/013
EU/1/01/183/026
EU/1/01/183/027
EU/1/01/183/028
EU/1/01/183/029
EU/1/01/183/032

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27/04/2001
Date of latest renewal: 04/08/2006

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

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 40 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 40 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced in *Saccharomyces cerevisiae* (strain 2150-2-3) yeast by recombinant DNA technology.
The vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. See sections 4.3, 4.4 and 4.8.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection
Slightly opaque white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HBVAXPRO is indicated for the active immunisation against hepatitis B virus infection caused by all known subtypes in predialysis and dialysis adult patients.

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

4.2 Posology and method of administration

Posology
Predialysis and dialysis adult patients: 1 dose (1 ml) at each injection.

Primary vaccination:

A course of vaccination should include three injections:
Schedule 0, 1, 6 months: two injections with an interval of one month; a third injection 6 months after the first administration.

Booster:

A booster dose must be considered in these vaccinees if the antibody level against hepatitis B virus surface antigen (anti-HBsAg) after primary series is less than 10 IU/l.

In accordance with standard medical practice for hepatitis B vaccine administration, regular antibody testing should be done in hemodialysis patients. A booster dose should be given when antibody levels decline below 10 IU/l.

Special dosage recommendations for known or presumed exposure to hepatitis B virus (e.g needlestick with contaminated needle):

- Hepatitis B immunoglobulin should be given as soon as possible after exposure (within 24 hours).
- The first dose of the vaccine should be given within 7 days of exposure and can be administered simultaneously with hepatitis B immunoglobulin but at a separate injection site.
- Serologic testing is also recommended, with the administration of subsequent doses of vaccine, if necessary, (i.e according to the serologic status of the patient) for short and long term protection.
- In the case of unvaccinated or incompletely vaccinated individuals, additional doses should be given as in the recommended immunisation schedule.

Method of administration

This vaccine should be administered intramuscularly.

The deltoid muscle is the preferred site for injection in adults.

Do not inject intravascularly.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia or bleeding disorders.

Precautions to be taken before handling or administering the product: see section 6.6.

For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- History of hypersensitivity to the active substance, or to any of the excipients, or trace residuals (e.g. formaldehyde and potassium thiocyanate) (see sections 6.1 and 2)
- Vaccination should be postponed in individuals with a severe febrile illness or acute infection.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine (see section 4.8).

This vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process. Therefore, hypersensitivity reactions may occur (see sections 2 and 4.8).

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 HBVAXPRO. Additional doses may need to be considered for persons who do not respond or have a sub-optimal response to a course of vaccinations.

Because of the long incubation period of hepatitis B, it is possible for unrecognised hepatitis B infection to be present at the time of vaccination. 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 and other pathogens known to infect the liver.

Caution should be exercised when prescribing to pregnant or breastfeeding women. (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

This vaccine can be administered:
- with hepatitis B immunoglobulin, at a separate injection site.
- to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
- concomitantly with other vaccines, using separate sites and syringes.

4.6 Fertility, pregnancy and lactation

Fertility:
HBVAXPRO has not been evaluated in fertility studies.

Pregnancy:
There is no clinical data on the use of HBVAXPRO on pregnant women.
The vaccine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breastfeeding:
There is no clinical data on the use of HBVAXPRO on breastfeeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most common side effects seen are injection-site reactions: transient soreness, erythema, induration.

b. Tabulated summary of adverse reactions

The following undesirable effects have been reported following the widespread use of the vaccine.

As with other hepatitis B vaccines, in many instances, the causal relationship to the vaccine has not been established.

Adverse reactions	Frequency
General disorders and administration site conditions	
Local reactions (injection site): Transient soreness, Erythema, Induration	Common (≥1/100 to, <1/10)

Fatigue, Fever, Malaise, Influenza-like symptoms	Very rare (<1/10,000)
Blood and the lymphatic system disorders	
Thrombocytopenia, Lymphadenopathy	Very rare (<1/10,000)
Immune system disorders	
Serum sickness, Anaphylaxis, Polyarteritis nodosa	Very rare (<1/10,000)
Nervous system disorders	
Paresthesia, Paralysis (including Bell's palsy, facial paralysis), Peripheral neuropathies (polyradiculoneuritis, Guillain Barre Syndrome), Neuritis (including optical neuritis), Myelitis (including transverse Myelitis), Encephalitis, Demyelinating disease of the central nervous system, Exacerbation of multiple sclerosis, Multiple sclerosis, Seizure, Headache, Dizziness, Syncope	Very rare (<1/10,000)
Vascular disorders	
Hypotension, Vasculitis	Very rare (<1/10,000)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm-like symptoms	Very rare (<1/10,000)
Gastrointestinal disorders	
Vomiting, Nausea, Diarrhoea, Abdominal pain	Very rare (<1/10,000)
Skin and subcutaneous tissue disorders	
Rash, Alopecia, Pruritus, Urticaria, Erythema multiforme, Angioedema, Eczema	Very rare (<1/10,000)
Musculoskeletal, connective tissue and bone disorders	
Arthralgia, Arthritis, Myalgia, Pain in extremity	Very rare (<1/10,000)
Investigations	
Elevation of liver enzymes	Very rare (<1/10,000)

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectious, ATC code: J07BC01

The vaccine induces specific humoral antibodies against hepatitis B virus surface antigen (anti-HBsAg). Development of an antibody titre against hepatitis B virus surface antigen (anti-HBsAg) equal to or greater than 10 IU/l measured 1 to 2 months after the last injection correlates with protection to hepatitis B virus infection.

In clinical trials, 96 % of 1,497 healthy infants, children, adolescents and adults given a 3 dose course of a previous formulation of Merck's recombinant hepatitis B vaccine developed a protective level of antibodies against hepatitis B virus surface antigen (≥ 10 IU/l).

Although the duration of the protective effect of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy vaccinees is unknown, follow-up over 5-9 years of approximately 3,000 high-risk subjects given a similar plasma-derived vaccine has revealed no cases of clinically apparent hepatitis B infection.

In addition, persistence of vaccine-induced immunologic memory for hepatitis B virus surface antigen (HBsAg) has been demonstrated through an anamnestic antibody response to a booster dose of a previous formulation of Merck's recombinant hepatitis B vaccine in healthy adults.

In accordance with standard medical practice for hepatitis B vaccine administration, regular antibody testing should be done in hemodialysis patients. A booster dose should be given when antibody levels decline below 10 IU/l. In subjects in whom insufficient antibody titres are achieved after boosting, the use of alternative hepatitis B vaccines should be considered.

Reduced risk of Hepatocellular Carcinoma
Hepatocellular carcinoma is a serious complication of hepatitis B virus infection. Studies have demonstrated the link between chronic hepatitis B infection and hepatocellular carcinoma and 80 % of hepatocellular carcinomas are caused by hepatitis B virus infection. Hepatitis B vaccine has been recognized as the first anti-cancer vaccine because it can prevent primary liver cancer.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Animal reproduction studies have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Borax
Water for injections.

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.

6.5 Nature and contents of container

1 ml of suspension in vial (glass) with stopper (gray butyl rubber) and aluminum seals with plastic flip caps. Pack size of 1.

6.6 Special precautions for disposal and other handling

The vaccine should be inspected visually in order to detect any appearance of precipitate or discolouring of the content prior to administration. If these conditions exist, the product should not be administered.
Before use, the vial should be well shaken.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/015

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27/04/2001
Date of latest renewal: 04/08/2006

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(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance

Merck Sharp & Dohme Corp.
Sumneytown Pike
West POINT,
Pennsylvania 19486
USA

Name and address of the manufacturer(s) responsible for batch release

MERCK Sharp & Dohme B.V.
Waaderweg 39,
2031 BN Haarlem
The Netherlands

B CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription

- **OTHER CONDITIONS**

Pharmacovigilance system

The MAH must ensure that the system of pharmacovigilance presented in Module 1.8.1. of the Marketing Authorisation, is in place and functioning before and whilst the product is on the market.

Official batch release: in accordance with Article 114 of Directive 2001/83/EC as amended, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose
PSUR: The marketing authorisation holder will continue to submit periodic safety update reports on a 1-year cycle.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 5 micrograms - single dose vial - Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 0.5 ml vial
10 single doses 0.5 ml vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/001 – pack of 1
EU/1/01/183/018 – pack of 10

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 5 micrograms - single dose vial + syringe with needle - Pack of 1

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 0.5 ml vial
1 sterile injection syringe with needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/019 – Pack of 1

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

HBVAXPRO 5 micrograms

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

HBVAXPRO 5 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

IM use

2. METHOD OF ADMINISTRATION

Shake well before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

SANOFI PASTEUR MSD SNC

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 5 micrograms - single dose pre-filled syringe without needle - Pack of 1, 10, 20, 50

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 0.5 ml pre-filled syringe without needle
10 single dose 0.5 ml pre-filled syringes without needle
20 single dose 0.5 ml pre-filled syringes without needle
50 single dose 0.5 ml pre-filled syringes without needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/004 – pack of 1
EU/1/01/183/005 – pack of 10
EU/1/01/183/020 – pack of 20
EU/1/01/183/021 – pack of 50

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 5 micrograms - single dose pre-filled syringe with 1 separate needle - Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 0.5 ml pre-filled syringe with 1 separate needle
10 single dose 0.5 ml pre-filled syringes with 1 separate needle (for each syringe)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/022 – pack of 1
EU/1/01/183/023 – pack of 10

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 5 micrograms - single dose pre-filled syringe with 2 separate needles - Pack of 1, 10, 20, 50

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 5 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 0.5 ml pre-filled syringe with 2 separate needles
10 single dose 0.5 ml pre-filled syringes with 2 separate needles (for each syringe)
20 single dose 0.5 ml pre-filled syringes with 2 separate needles (for each syringe)
50 single dose 0.5 ml pre-filled syringes with 2 separate needles (for each syringe)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/024 – pack of 1
EU/1/01/183/025 – pack of 10
EU/1/01/183/030 – pack of 20
EU/1/01/183/031 – pack of 50

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the

packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

HBVAXPRO 5 micrograms

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

HBVAXPRO 5 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

IM use

2. METHOD OF ADMINISTRATION

Shake well before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

SANOFI PASTEUR MSD SNC

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 10 micrograms - single dose vial - Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 10 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 1 ml vial.
10 single dose 1 ml vials.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/007 – pack of 1
EU/1/01/183/008 – pack of 10

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

HBVAXPRO 10 micrograms

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

HBVAXPRO 10 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

IM use

2. METHOD OF ADMINISTRATION

Shake well before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

SANOFI PASTEUR MSD SNC

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 10 micrograms - single dose pre-filled syringe without needle - Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 10 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 1 ml pre-filled syringe without needle
10 single dose 1 ml pre-filled syringes without needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/011 – pack of 1
EU/1/01/183/013 – pack of 10

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 10 micrograms - single dose pre-filled syringe with 1 separate needle - Pack of 1, 10

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 10 micrograms, suspension for injection in pre-filled syringe

Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) *..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 1 ml pre-filled syringe with 1 separate needle
10 single dose 1 ml pre-filled syringes with 1 separate needle (for each syringe)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/026 – pack of 1
EU/1/01/183/027 – pack of 10

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 10 micrograms - single dose pre-filled syringe with 2 separate needles - Pack of 1, 10, 20

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 10 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10.00 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 1 ml pre-filled syringe with 2 separate needles
10 single dose 1 ml pre-filled syringes with 2 separate needles (for each syringe)
20 single dose 1 ml pre-filled syringes with 2 separate needles (for each syringe)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/028 – pack of 1
EU/1/01/183/029 – pack of 10
EU/1/01/183/032 – pack of 20

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

HBVAXPRO 10 micrograms

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

HBVAXPRO 10 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

IM use

2. METHOD OF ADMINISTRATION

Shake well before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

SANOFI PASTEUR MSD SNC

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

HBVAXPRO 40 micrograms - single dose vial - Pack of 1

1. NAME OF THE MEDICINAL PRODUCT

HBVAXPRO 40 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1 ml) contains:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 40 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

3. LIST OF EXCIPIENTS

Sodium chloride, borax and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 single dose 1 ml vial.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze

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

SANOFI PASTEUR MSD SNC
8, rue Jonas Salk
F-69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/01/183/015

13. MANUFACTURER'S BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

According to the Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended), there is no need to put the name in Braille on the packaging of products which are only intended for administration by health care professionals, for example it is not required to put the name in Braille for vaccines.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

HBVAXPRO 40 micrograms

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

HBVAXPRO 40 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

IM use

2. METHOD OF ADMINISTRATION

Shake well before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

SANOFI PASTEUR MSD SNC

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

HBVAXPRO 5 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

Read all of this leaflet carefully before your child is vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT HBVAXPRO 5 micrograms IS AND WHAT IT IS USED FOR

This vaccine is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals from birth through 15 years of age considered at risk of exposure to hepatitis B virus.

It can be expected that hepatitis D will also be prevented by immunisation with HBVAXPRO as hepatitis D does not occur in the absence of hepatitis B infection.

The vaccine 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.

2. BEFORE YOU OR YOUR CHILD RECEIVE HBVAXPRO 5 micrograms

Do not use HBVAXPRO 5 micrograms:
- if your child is allergic (hypersensitive) to hepatitis B surface antigen or to any of the other ingredients of HBVAXPRO (see section 6.)
- if your child has a severe illness with fever

Using other vaccines:
HBVAXPRO can be administered at the same time as with hepatitis B immunoglobulin, at a separate injection site.
HBVAXPRO can be used to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
HBVAXPRO may be administered at the same time as with some other vaccines, using separate sites and syringes.

Please tell your doctor or pharmacist if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

Caution should be exercised when prescribing the vaccine to pregnant or breastfeeding women.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

Important information about some of the ingredients of HBVAXPRO 5 micrograms:
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium-free".

3. HOW HBVAXPRO 5 micrograms IS GIVEN:

Dosage:

The recommended dose for each injection (0.5 ml) is 5 micrograms for individuals from birth through 15 years of age.

A course of vaccination should include at least three injections.

Two immunisation schedules can be recommended:
- two injections with an interval of one month followed by a third injection 6 months after the first administration (0,1,6 months).
- if immunity is needed quickly: three injections with an interval of one month and a fourth dose 1 year later (0,1,2,12 months).

In case of a recent exposure to the hepatitis B virus, a first dose of HBVAXPRO together with the appropriate dose of immunoglobulin can be given.

Some local vaccination schedules currently include recommendations for a booster dose. Your doctor or pharmacist will inform you if a booster dose should be given.

Method of administration:

The vial should be well shaken until a slightly opaque white suspension is obtained.
Once the vial has been penetrated, the withdrawn vaccine should be used promptly, and the vial must be discarded.
The doctor will give the vaccine as an injection into muscle. The upper side of the thigh is the preferred site for injection in neonates and infants. The upper arm muscle is the preferred site for injection in children and adolescents.

This vaccine should never be given into a blood vessel.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia (diminution of blood platelets) or to persons at risk of haemorrhage.

If you forget one dose of HBVAXPRO 5 micrograms:

If you miss a scheduled injection, talk to your doctor. Your doctor will decide when to give the missed dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

As with other hepatitis B vaccines, in many instances, the causal relationship of side effects to the vaccine has not been established.

The most common side effects seen are injection-site reactions: soreness, redness and hardening.

Other side effects are reported very rarely:

- Low platelet count, Lymph node disease
- Allergic reactions
- Nervous system disorders such as pins and needles, Facial paralysis, Nerve inflammations including Guillain-Barre Syndrome, Inflammation of the nerve of the eye that leads to impaired vision, Brain inflammation, Exacerbation of multiple sclerosis, Multiple sclerosis, Convulsions, Headache, Dizziness and Fainting
- Low blood pressure, Blood vessel inflammation
- Asthma-like symptoms
- Vomiting, Nausea, Diarrhoea, Abdominal pain
- Skin reactions such as eczema, Rash, Itching, Hives and Skin blistering, Hair loss
- Joint pain, Arthritis, Muscle pain, Pain in extremity
- Fatigue, Fever, Vague illness, Flu-like symptoms
- Elevation of liver enzymes

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE HBVAXPRO 5 micrograms

Keep out of the reach and sight of children.

Do not use HBVAXPRO after the expiry date which is stated on the label.

Store in a refrigerator between 2°C and 8°C
Do not freeze

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What HBVAXPRO 5 micrograms contains

The active substance is :

Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

The other ingredients are sodium chloride, borax and water for injections.

What HBVAXPRO 5 micrograms looks like and contents of the pack

HBVAXPRO 5 micrograms is a suspension for injection in a vial.
Pack sizes of 1 and 10 vials without syringe/needle.
Pack size of 1 vial with syringe and needle.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Sanofi Pasteur MSD SNC
8 rue Jonas Salk
F-69007 Lyon
France

Manufacturer Responsible for Batch Release:
Merck Sharp and Dohme, B.V.
Waarderweg, 39
2031 BN Haarlem
The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien

Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

Luxembourg/Luxemburg

Sanofi Pasteur MSD, Tél: +32.2.726.95.84

България

Мерк Шарп и Доум България ЕООД тел. + 359 2 819 3740

Magyarország

MSD Magyarország Kft, Tel.: + 36.1.888.5300

Česká republika

Merck Sharp & Dohme IDEA, Inc., org. sl., Tel.: +420.233.010.111

Malta

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Danmark

Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Nederland

Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Deutschland

Sanofi Pasteur MSD GmbH, Tel: +49.6224.5940

Norge

Sanofi Pasteur MSD, Tlf: +47.67.50.50.20

Eesti

Merck Sharp & Dohme OÜ, Tel: +372.613.9750

Ελλάδα

BIANEΞ A.E., Τηλ: +30.210.8009111

España

Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00

France

Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00

Ireland

Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland

Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia

Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11

Κύπρος

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Latvija

SIA Merck Sharp & Dohme Latvija, Tel: +371.67364.224

Lietuva

UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

Österreich

Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91 1

Polska

MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00

Portugal

Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50

România

Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00

Slovenija

Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201

Slovenská republika

Merck Sharp & Dohme IDEA, Inc., Tel: +421.2.58282010

Suomi/Finland

Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30

Sverige

Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom

Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last approved in …….

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

PACKAGE LEAFLET: INFORMATION FOR THE USER

HBVAXPRO 5 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

Read all of this leaflet carefully before your child is vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT HBVAXPRO 5 micrograms IS AND WHAT IT IS USED FOR

This vaccine is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals from birth through 15 years of age considered at risk of exposure to hepatitis B virus.

It can be expected that hepatitis D will also be prevented by immunisation with HBVAXPRO as hepatitis D does not occur in the absence of hepatitis B infection.

The vaccine 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.

2. BEFORE YOU OR YOUR CHILD RECEIVE HBVAXPRO 5 micrograms

Do not use HBVAXPRO 5 micrograms:
- if your child is allergic (hypersensitive) to hepatitis B surface antigen or to any of the other ingredients of HBVAXPRO (see section 6.)
- if your child has a severe illness with fever

Using other vaccines:
HBVAXPRO can be administered at the same time as with hepatitis B immunoglobulin, at a separate injection site.
HBVAXPRO can be used to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
HBVAXPRO may be administered at the same time as with some other vaccines, using separate sites and syringes.

Please tell your doctor or pharmacist if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding
Caution should be exercised when prescribing the vaccine to pregnant or breastfeeding women.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

Important information about some of the ingredients of HBVAXPRO 5 micrograms:
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium-free".

3. HOW HBVAXPRO 5 micrograms IS GIVEN:

Dosage:

The recommended dose for each injection (0.5 ml) is 5 micrograms for individuals from birth through 15 years of age.

A course of vaccination should include at least three injections.

Two immunisation schedules can be recommended:
- two injections with an interval of one month followed by a third injection 6 months after the first administration (0,1,6 months).
- if immunity is needed quickly: three injections with an interval of one month and a fourth dose 1 year later (0,1,2,12 months).

In case of a recent exposure to the hepatitis B virus, a first dose of HBVAXPRO together with the appropriate dose of immunoglobulin can be given.

Some local vaccination schedules currently include recommendations for a booster dose. Your doctor or pharmacist will inform you if a booster dose should be given.

Method of administration:

The doctor will give the vaccine as an injection into muscle. The upper side of the thigh is the preferred site for injection in neonates and infants. The upper arm muscle is the preferred site for injection in children and adolescents.

This vaccine should never be given into a blood vessel.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia (diminution of blood platelets) or to persons at risk of haemorrhage.

If you forget one dose of HBVAXPRO 5 micrograms:

If you miss a scheduled injection, talk to your doctor. Your doctor will decide when to give the missed dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

As with other hepatitis B vaccines, in many instances, the causal relationship of side effects to the vaccine has not been established.

The most common side effects seen are injection-site reactions: soreness, redness and hardening.

Other side effects are reported very rarely:

- Low platelet count, Lymph node disease
- Allergic reactions
- Nervous system disorders such as pins and needles, Facial paralysis, Nerve inflammations including Guillain-Barre Syndrome, Inflammation of the nerve of the eye that leads to impaired vision, Brain inflammation, Exacerbation of multiple sclerosis, Multiple sclerosis, Convulsions, Headache, Dizziness and Fainting
- Low blood pressure, Blood vessel inflammation
- Asthma-like symptoms
- Vomiting, Nausea, Diarrhoea, Abdominal pain
- Skin reactions such as eczema, Rash, Itching, Hives and Skin blistering, Hair loss
- Joint pain, Arthritis, Muscle pain, Pain in extremity
- Fatigue, Fever, Vague illness, Flu-like symptoms
- Elevation of liver enzymes

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE HBVAXPRO 5 micrograms

Keep out of the reach and sight of children.

Do not use HBVAXPRO after the expiry date which is stated on the label.

Store in a refrigerator between 2°C and 8°C

Do not freeze

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What HBVAXPRO 5 micrograms contains

The active substance is:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 5 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.25 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

The other ingredients are sodium chloride, borax and water for injections.

What HBVAXPRO 5 micrograms looks like and contents of the pack

HBVAXPRO 5 micrograms is a suspension for injection in a syringe.
Pack sizes of 1, 10, 20 and 50 pre-filled syringes without needle or with 2 separate needles,
Pack sizes of 1 and 10 pre-filled syringes with 1 separate needle.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Sanofi Pasteur MSD SNC
8 rue Jonas Salk
F-69007 Lyon
France

Manufacturer Responsible for Batch Release:
Merck Sharp and Dohme, B.V.
Waarderweg, 39
2031 BN Haarlem
The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien

Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

Luxembourg/Luxemburg

Sanofi Pasteur MSD, Tél: +32.2.726.95.84

България

Мерк Шарп и Доум България ЕООД тел. + 359 2 819 3740

Magyarország

MSD Magyarország Kft, Tel.: + 36.1.888.5300

Česká republika

Merck Sharp & Dohme IDEA, Inc., org. sl., Tel.: +420.233.010.111

Malta

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Danmark

Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Nederland

Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Deutschland

Sanofi Pasteur MSD GmbH, Tel: +49.6224.5940

Norge

Sanofi Pasteur MSD, Tlf: +47.67.50.50.20

Eesti

Österreich

Merck Sharp & Dohme OÜ, Tel: +372.613.9750

Ελλάδα

BIANEΞ A.E., Τηλ: +30.210.8009111

España

Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00

France

Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00

Ireland

Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland

Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia

Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11

Κύπρος

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Latvija

SIA Merck Sharp & Dohme Latvija, Tel: +371.67364.224

Lietuva

UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91 1

Polska

MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00

Portugal

Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50

România

Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00

Slovenija

Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201

Slovenská republika

Merck Sharp & Dohme IDEA, Inc., Tel: +421.2.58282010

Suomi/Finland

Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30

Sverige

Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom

Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last approved in …….

The following information is intended for medical or health care professionals only:

Instructions

The vaccine should be inspected visually prior to administration for any foreign particulate matter and/or abnormal physical appearance. The syringe should be well shaken until a slightly opaque white suspension is obtained.
The needle is attached by twisting in clockwise direction, until the needle fits securely on the syringe.

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

PACKAGE LEAFLET: INFORMATION FOR THE USER

HBVAXPRO 10 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

Read all of this leaflet carefully before you are vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT HBVAXPRO 10 micrograms IS AND WHAT IT IS USED FOR

This vaccine is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals 16 years of age or more considered at risk of exposure to hepatitis B virus.

It can be expected that hepatitis D will also be prevented by immunisation with HBVAXPRO as hepatitis D does not occur in the absence of hepatitis B infection.

The vaccine 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.

2. BEFORE YOU RECEIVE HBVAXPRO 10 micrograms

Do not use HBVAXPRO 10 micrograms:
- if you are allergic (hypersensitive) to hepatitis B surface antigen or to any of the other ingredients of HBVAXPRO (see section 6.)
- if you have a severe illness with fever

Take special care with HBVAXPRO 10 micrograms:

Using other vaccines:
HBVAXPRO can be administered at the same time as with hepatitis B immunoglobulin, at a separate injection site.
HBVAXPRO can be used to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
HBVAXPRO can be administered at the same time as other vaccines, using separate sites and syringes.

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription

Pregnancy and Breast-feeding:

Caution should be exercised when prescribing the vaccine to pregnant or breastfeeding women.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

Important information about some of the ingredients of HBVAXPRO 10 micrograms~~/ml~~:
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium-free".

.

3. HOW HBVAXPRO 10 micrograms IS GIVEN

Dosage:

The recommended dose for each injection (1 ml) is 10 micrograms for individuals 16 years of age or more.

A course of vaccination should include three injections.

Two immunisation schedules can be recommended:
- two injections with an interval of one month followed by a third injection 6 months after the first administration (0,1,6 months)
- if immunity is needed quickly: three injections with an interval of one month and a fourth dose 1 year later (0,1,2,12 months).

In case of a recent exposure to the hepatitis B virus, a first dose of HBVAXPRO together with the appropriate dose of immunoglobulin can be given.

Some local vaccination schedules currently include recommendations for a booster dose. Your doctor or pharmacist will inform you if a booster dose should be given.

For individuals less than 16 years of age, HBVAXPRO 10 micrograms is not recommended. The appropriate strength for administration to individuals from birth through 15 years of age is HBVAXPRO 5 micrograms.

Method of administration:

The vial should be well shaken until a slightly opaque white suspension is obtained.
The doctor will give the vaccine as an injection into muscle. The upper arm muscle is the preferred site for injection in adults and adolescents.
This vaccine should never be given into a blood vessel.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia (diminution of blood platelets) or to persons at risk of haemorrhage.

If you forget one dose of HBVAXPRO 10 micrograms:

If you missed a scheduled injection, talk to your doctor. Your doctor will decide when to give the missed dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

As with other hepatitis B vaccines, in many instances, the causal relationship of side effects to the vaccine has not been established.

The most common side effects seen are injection-site reactions: soreness, redness and hardening.

Other side effects are reported very rarely:

- Low platelet count, Lymph node disease
- Allergic reactions
- Nervous system disorders such as pins and needles, Facial paralysis, Nerve inflammations including Guillain-Barre Syndrome, Inflammation of the nerve of the eye that leads to impaired vision, Brain inflammation, Exacerbation of multiple sclerosis, Multiple sclerosis, Convulsions, Headache, Dizziness and Fainting
- Low blood pressure, Blood vessel inflammation
- Asthma-like symptoms
- Vomiting, Nausea, Diarrhoea, Abdominal pain
- Skin reactions such as eczema, Rash, Itching, Hives and Skin blistering, Hair loss
- Joint pain, Arthritis, Muscle pain, Pain in extremity
- Fatigue, Fever, Vague illness, Flu-like symptoms
- Elevation of liver enzymes

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE HBVAXPRO 10 micrograms

Keep out of the reach and sight of children.

Do not use HBVAXPRO after the expiry date which is stated on the label.

Store in a refrigerator between 2°C and 8°C
Do not freeze

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What HBVAXPRO 10 micrograms contains

The active substance is:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

The other ingredients are sodium chloride, borax and water for injections.

What HBVAXPRO 10 micrograms looks like and contents of the pack

HBVAXPRO 10 micrograms is a suspension for injection in a vial.
Pack sizes of 1 and 10 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Sanofi Pasteur MSD SNC
8 rue Jonas Salk
F-69007 Lyon
France

Manufacturer Responsible for Batch Release:
Merck Sharp and Dohme, B.V.
Waarderweg, 39
2031 BN Haarlem
The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien

Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

Luxembourg/Luxemburg

Sanofi Pasteur MSD, Tél: +32.2.726.95.84

България

Мерк Шарп и Доум България ЕООД тел. + 359 2 819 3740

Magyarország

MSD Magyarország Kft, Tel.: + 36.1.888.5300

Česká republika

Merck Sharp & Dohme IDEA, Inc., org. sl., Tel.: +420.233.010.111

Malta

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Danmark

Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Nederland

Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Deutschland

Sanofi Pasteur MSD GmbH, Tel: +49.6224.5940

Norge

Sanofi Pasteur MSD, Tlf: +47.67.50.50.20

Eesti

Österreich

Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91

Merck Sharp & Dohme OÜ, Tel: +372.613.9750 1

Ελλάδα

BIANEΞ A.E., Τηλ: +30.210.8009111

España

Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00

France

Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00

Ireland

Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland

Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia

Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11

Κύπρος

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Latvija

SIA Merck Sharp & Dohme Latvija, Tel: +371.67364.224

Lietuva

UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

Polska

MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00

Portugal

Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50

România

Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00

Slovenija

Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201

Slovenská republika

Merck Sharp & Dohme IDEA, Inc., Tel: +421.2.58282010

Suomi/Finland

Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30

Sverige

Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom

Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last approved in …….

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

PACKAGE LEAFLET: INFORMATION FOR THE USER

HBVAXPRO 10 micrograms, suspension for injection in pre-filled syringe
Hepatitis B vaccine (rDNA)

Read all of this leaflet carefully before you are vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT HBVAXPRO 10 micrograms IS AND WHAT IT IS USED FOR

This vaccine is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in individuals 16 years of age or more considered at risk of exposure to hepatitis B virus.

It can be expected that hepatitis D will also be prevented by immunisation with HBVAXPRO as hepatitis D does not occur in the absence of hepatitis B infection.

The vaccine 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.

2. BEFORE YOU RECEIVE HBVAXPRO 10 micrograms

Do not use HBVAXPRO 10 micrograms:
- if you are allergic (hypersensitive) to hepatitis B surface antigen or to any of the other ingredients of HBVAXPRO (see section 6.)
- if you have a severe illness with fever

Take special care with HBVAXPRO 10 micrograms:

Using other vaccines:
HBVAXPRO can be administered at the same time as with hepatitis B immunoglobulin, at a separate injection site.
HBVAXPRO can be used to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
HBVAXPRO can be administered at the same time as with other vaccines, using separate sites and syringes.

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and Breast-feeding:
Caution should be exercised when prescribi
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

Important information about some of the ingredients of HBVAXPRO 10 micrograms~~/ml~~:
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium- free.

3. HOW HBVAXPRO 10 micrograms IS GIVEN:

Dosage:

The recommended dose for each injection (1 ml) is 10 micrograms for individuals 16 years of age or more.

A course of vaccination should include at least three injections.

Two immunisation schedules can be recommended:
- two injections with an interval of one month followed by a third injection 6 months after the first administration (0,1,6 months)
- if immunity is needed quickly: three injections with an interval of one month and a fourth dose 1 year later (0,1,2,12 months).

In case of a recent exposure to the hepatitis B virus, a first dose of HBVAXPRO together with the appropriate dose of immunoglobulin can be given.

Some local vaccination schedules currently include recommendations for a booster dose. Your doctor or pharmacist will inform you if a booster dose should be given.

For individuals less than 16 years of age, HBVAXPRO 10 micrograms is not recommended. The appropriate strength for administration to individuals from birth to 15 years of age is HBVAXPRO 5 micrograms.

Method of administration:

The doctor will give the vaccine as an injection into muscle. The upper arm muscle is the preferred site for injection in adults and adolescents.

This vaccine should never be given into a blood vessel.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia (diminution of blood platelets) or to persons at risk of haemorrhage.

If you forget one dose of HBVAXPRO 10 micrograms:

If you miss a scheduled injection, talk to your doctor. Your doctor will decide when to give the missed dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

As with other hepatitis B vaccines, in many instances, the causal relationship of side effects to the vaccine has not been established.

The most common side effects seen are injection-site reactions: soreness, redness and hardening.

Other side effects are reported very rarely:

- Low platelet count, Lymph node disease
- Allergic reactions
- Nervous system disorders such as pins and needles, Facial paralysis, Nerve inflammations including Guillain-Barre Syndrome, Inflammation of the nerve of the eye that leads to impaired vision, Brain inflammation, Exacerbation of multiple sclerosis, Multiple sclerosis, Convulsions, Headache, Dizziness and Fainting
- Low blood pressure, Blood vessel inflammation
- Asthma-like symptoms
- Vomiting, Nausea, Diarrhoea, Abdominal pain
- Skin reactions such as eczema, Rash, Itching, Hives and Skin blistering, Hair loss
- Joint pain, Arthritis, Muscle pain, Pain in extremity
- Fatigue, Fever, Vague illness, Flu-like symptoms
- Elevation of liver enzymes

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE HBVAXPRO 10 micrograms

Keep out of the reach and sight of children.

Do not use HBVAXPRO after the expiry date which is stated on the label.

Store in a refrigerator between 2°C and 8°C
Do not freeze

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What HBVAXPRO 10 micrograms contains

The active substance is:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 10 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

The other ingredients are sodium chloride, borax and water for injections.

What HBVAXPRO 10 micrograms looks like and contents of the pack

HBVAXPRO 10 micrograms is a suspension for injection in a syringe.
Pack sizes of 1, 10 and 20 pre-filled syringes with 2 separate needles.
Pack sizes of 1 and 10 pre-filled syringes without needle, or with 1 separate needle.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Sanofi Pasteur MSD SNC
8 rue Jonas Salk
F-69007 Lyon
France

Manufacturer Responsible for Batch Release:
Merck Sharp and Dohme, B.V.
Waarderweg, 39
2031 BN Haarlem
The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien

Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

Luxembourg/Luxemburg

Sanofi Pasteur MSD, Tél: +32.2.726.95.84

България

Мерк Шарп и Доум България ЕООД тел. + 359 2 819 3740

Magyarország

MSD Magyarország Kft, Tel.: + 36.1.888.5300

Česká republika

Merck Sharp & Dohme IDEA, Inc., org. sl., Tel.: +420.233.010.111

Malta

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Danmark

Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Nederland

Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Deutschland

Sanofi Pasteur MSD GmbH, Tel: +49.6224.5940

Norge

Sanofi Pasteur MSD, Tlf: +47.67.50.50.20

Eesti

Österreich

Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91

Merck Sharp & Dohme OÜ, Tel: +372.613.9750 1

Ελλάδα

BIANEΞ A.E., Τηλ: +30.210.8009111

España

Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00

France

Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00

Ireland

Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland

Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia

Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11

Κύπρος

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Latvija

SIA Merck Sharp & Dohme Latvija, Tel: +371.67364.224

Lietuva

UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

Polska

MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00

Portugal

Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50

România

Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00

Slovenija

Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201

Slovenská republika

Merck Sharp & Dohme IDEA, Inc., Tel: +421.2.58282010

Suomi/Finland

Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30

Sverige

Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom

Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last approved in ……..

The following information is intended for medical or health care professionals only:

Instructions

The vaccine should be inspected visually prior to administration for any foreign particulate matter and/or abnormal physical appearance.The syringe should be well shaken until a slightly opaque white suspension is obtained.

The needle is attached by twisting in clockwise direction, until the needle fits securely on the syringe.

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

PACKAGE LEAFLET: INFORMATION FOR THE USER

HBVAXPRO 40 micrograms, suspension for injection
Hepatitis B vaccine (rDNA)

Read all of this leaflet carefully before you are vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT HBVAXPRO 40 micrograms IS AND WHAT IT IS USED FOR

This vaccine is indicated for active immunisation against hepatitis B virus infection caused by all known subtypes in predialysis and dialysis adult patients.

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

The vaccine 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.

2. BEFORE YOU USE HBVAXPRO 40 micrograms

Do not use HBVAXPRO 40 micrograms:
- if you are allergic (hypersensitive) to hepatitis B surface antigen or to any of the other ingredients of HBVAXPRO (see section 6.)
- if you have a severe illness with fever

Take special care with HBVAXPRO 40 micrograms:

Using other vaccines:
HBVAXPRO can be administered at the same time as with hepatitis B immunoglobulin, at a separate injection site.
HBVAXPRO can be used to complete a primary immunisation course or as a booster dose in subjects who have previously received another hepatitis B vaccine.
HBVAXPRO can be administered at the same time as with other vaccines, using separate sites and syringes.

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and Breast-feeding:
Caution should be exercised when prescribing the vaccine to pregnant or breastfeeding women.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
HBVAXPRO is expected to have no or negligible influence on the ability to drive and use machines.

Important information about some of the ingredients of HBVAXPRO 40 micrograms~~/ml~~:
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium- free.

3. HOW HBVAXPRO 40 micrograms IS GIVEN:

Dosage:

The recommended dose for each injection (1 ml) is 40 micrograms for predialysis and dialysis adult patients

A course of vaccination should include three injections.

The schedule is two injections with an interval of one month followed by a third injection 6 months after the first administration (0,1,6 months).

A booster dose must be considered in these vaccinees if the antibody level against hepatitis B virus surface antigen is less than 10 IU/l.

Method of administration:

The vial should be well shaken until a slightly opaque white suspension is obtained.
The doctor will give the vaccine as an injection into muscle. The upper arm muscle is the preferred site for injection in adults.

This vaccine should never be given into a blood vessel.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopoenia (diminution of blood platelets) or to persons at risk of haemorrhage.

If you forget one dose of HBVAXPRO 40 micrograms:

If you miss a scheduled injection, talk to your doctor. Your doctor will decide when to give the missed dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

As with other hepatitis B vaccines, in many instances, the causal relationship of side effects to the vaccine has not been established.

The most common side effects seen are injection-site reactions: soreness, redness and hardening.

Other side effects are reported very rarely:

- Low platelet count, Lymph node disease
- Allergic reactions
- Nervous system disorders such as pins and needles, Facial paralysis, Nerve inflammations including Guillain-Barre Syndrome, Inflammation of the nerve of the eye that leads to impaired vision, Brain inflammation, Exacerbation of multiple sclerosis, Multiple sclerosis, Convulsions, Headache, Dizziness and Fainting
- Low blood pressure, Blood vessel inflammation
- Asthma-like symptoms
- Vomiting, Nausea, Diarrhoea, Abdominal pain
- Skin reactions such as eczema, Rash, Itching, Hives and Skin blistering, Hair loss
- Joint pain, Arthritis, Muscle pain, Pain in extremity
- Fatigue, Fever, Vague illness, Flu-like symptoms
- Elevation of liver enzymes

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE HBVAXPRO 40 micrograms

Keep out of the reach and sight of children.

Do not use HBVAXPRO after the expiry date which is stated on the label.

Store in a refrigerator between 2°C and 8°C
Do not freeze

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What HBVAXPRO 40 micrograms contains

The active substance is:
Hepatitis B virus surface antigen, recombinant (HBsAg) * ..... 40 micrograms
Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.50 milligram Al^{+})

* produced from recombinant strain of the yeast *Saccharomyces cerevisiae* (strain 2150-2-3)

The other ingredients are sodium chloride, borax and water for injections.

What HBVAXPRO 40 micrograms looks like and contents of the pack

HBVAXPRO 40 micrograms is a suspension for injection in a vial.
Pack size of 1 vial.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Sanofi Pasteur MSD SNC
8 rue Jonas Salk
F-69007 Lyon
France

Manufacturer Responsible for Batch Release:
Merck Sharp and Dohme, B.V.
Waarderweg, 39
2031 BN Haarlem
The Netherlands

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

België/Belgique/Belgien

Sanofi Pasteur MSD, Tél/Tel: +32.2.726.95.84

Luxembourg/Luxemburg

Sanofi Pasteur MSD, Tél: +32.2.726.95.84

България

Мерк Шарп и Доум България ЕООД тел. + 359 2 819 3740

Magyarország

MSD Magyarország Kft, Tel.: + 36.1.888.5300

Česká republika

Merck Sharp & Dohme IDEA, Inc., org. sl., Tel.: +420.233.010.111

Malta

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Danmark

Sanofi Pasteur MSD, Tlf: +45 23 32 69 29

Nederland

Sanofi Pasteur MSD, Tel: +31.23.567.96.00

Deutschland

Sanofi Pasteur MSD GmbH, Tel: +49.6224.5940

Norge

Sanofi Pasteur MSD, Tlf: +47.67.50.50.20

Eesti

Merck Sharp & Dohme OÜ, Tel: +372.613.9750

Österreich

Sanofi Pasteur MSD GmbH, Tel: +43 1 890 34 91 1

Ελλάδα

BIANEΞ A.E., Τηλ: +30.210.8009111

Polska

MSD Polska Sp. z o.o., Tel.: +48.22.549.51.00

España

Sanofi Pasteur MSD S.A., Tel: +34.91.371.78.00

Portugal

Sanofi Pasteur MSD, SA, Tel: +351.21.470.45.50

France

Sanofi Pasteur MSD SNC, Tél: +33.4.37.28.40.00

Ireland

Sanofi Pasteur MSD Ltd, Tel: +3531.468.5600

Ísland

Sanofi Pasteur MSD, Sími: +32.2.726.95.84

Italia

Sanofi Pasteur MSD Spa, Tel: +39.06.664.092.11

Κύπρος

Merck Sharp & Dohme Cyprus Limited., Τηλ: +357 22866700

Latvija

SIA Merck Sharp & Dohme Latvija, Tel: +371.67364.224

Lietuva

UAB Merck Sharp & Dohme, Tel.: +370.5.2780.247

România

Merck Sharp & Dohme Romania S.R.L. Tel: + 4021 529 29 00

Slovenija

Merck Sharp & Dohme, inovativna zdravila d.o.o., Tel: +386.1.520.4201

Slovenská republika

Merck Sharp & Dohme IDEA, Inc., Tel: +421.2.58282010

Suomi/Finland

Sanofi Pasteur MSD, Puh/Tel: +358.9.565.88.30

Sverige

Sanofi Pasteur MSD, Tel: +46.8.564.888.60

United Kingdom

Sanofi Pasteur MSD Ltd, Tel: +44.1.628.785.291

This leaflet was last approved in …….

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