

# NEW ZEALAND DATA SHEET

## 1 PRODUCT NAME

HBvaxPRO® 5 mcg/0.5 mL Suspension for injection  
HBvaxPRO® 10 mcg/mL Suspension for injection  
HBvaxPRO® 40 mcg/mL Suspension for injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

*Hepatitis B vaccine (recombinant) injections*

5 mcg hepatitis B surface antigen per 0.5 mL (without preservative)  
10 mcg hepatitis B surface antigen per 1.0 mL (without preservative)  
40 mcg hepatitis B surface antigen per 1.0 mL (This formulation is intended for predialysis/dialysis patients only (without preservative))

The vaccine is available in 0.5 mL vials containing 5 mcg of hepatitis B surface antigen and in 1.0 mL vials containing 10 mcg of hepatitis B surface antigen\*.

The vaccine is also produced as a 1.0 mL vial containing 40 mcg of hepatitis B surface antigen\* for use in dialysis and predialysis patients.

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

Each 0.5 mL dose contains approximately 0.25 mg of aluminum provided as amorphous aluminum hydroxyphosphate sulfate adjuvant, and 35 mcg of sodium borate, 4.5 mg sodium chloride, and water for injection.

Each 1 mL dose contains approximately 0.5 mg of aluminum provided as amorphous aluminum hydroxyphosphate sulfate adjuvant, and 70 mcg of sodium borate, 9.0 mg sodium chloride, and water for injection.

The 5 mcg/0.5 mL, the 10 mcg/1.0 mL and the 40 mcg/1.0 mL formulations are only available without preservative. In each formulation, hepatitis B surface antigen is adsorbed onto approximately 0.5 mg of aluminium (provided as amorphous aluminium hydroxyphosphate sulphate adjuvant) per mL of vaccine. The vaccine is of the *adw* subtype.

This vaccine may contain traces of formaldehyde and potassium thiocyanate which are used during the manufacturing process.

For the full list of excipients, see Section 6.1 List of excipients.

## 3 PHARMACEUTICAL FORM

Suspension for injection

Slightly opaque white suspension

## 4 CLINICAL PARTICULARS

## 4.1 Therapeutic indications

All formulations of HBvaxPRO are indicated for immunisation against infection caused by all known subtypes of hepatitis B virus.

HBvaxPRO should also prevent hepatitis D (caused by the delta virus) since hepatitis D does not occur in the absence of hepatitis B infection.

## 4.2 Dose and method of administration

HBvaxPRO (hepatitis B [recombinant], MSD) (40 mcg/1.0 mL) (without preservative) is intended only for adult predialysis/dialysis patients.

HBvaxPRO (hepatitis B [recombinant], MSD) (5 mcg/0.5 mL [without preservative] or 10 mcg/1.0 mL [without preservative]) is not intended for use in dialysis/predialysis patients.

HBvaxPRO (hepatitis B vaccine [recombinant], MSD), (10 mcg/1.0 mL and 5 mcg/0.5 mL [without preservative]) is available for use in individuals for whom a thimerosal-free vaccine may be desired.

### Dose

#### Three-Dose Regimen

The vaccination regimen consists of three doses of vaccine given according to the following schedule:

First injection: at elected date

Second injection:  $\geq 1$  month after first injection

Third injection:  $\geq 1$  month after second injection

Within limits, the timing of successive injections may be adjusted to accommodate a variety of needs, such as co-administration with other EPI vaccines.

For infants born of mothers who are HBsAg positive or mothers of unknown HBsAg status, treatment recommendations are described in the subsections titled: 'Dosage Regimen for Infants Born to HBsAg Positive Mothers' and 'Dosage Regimen for Infants of Mothers of Unknown HBsAg Status'.

A minimum of one month should separate successive injections of vaccine. Accelerated three dose regimens (e.g. 0, 1, 2 months; 0, 2, 4 months) may induce protective antibody earlier in a slightly larger proportion of vaccinees. However, regimens that extend the time interval between the second and third injections (e.g. 0, 1, 6 months; 0, 1, 12 months) will ultimately seroconvert a similar proportion of vaccinees while inducing substantially higher antibody titres than accelerated regimens.

#### Two-Dose Regimen – Adolescents (11-15 years of age)

An alternate two-dose regimen is available for routine vaccination of adolescents (11 to 15 years of age). The regimen consists of two doses of vaccine (10 mcg) given according to the following schedule:

First injection: at elected date  
 Second injection: 4-6 months later

The dosing regimens of HBvaxPRO for specific populations other than predialysis/dialysis patients, regardless of the risk of infection with hepatitis B virus, are as follows:

GROUP	REGIMEN
Infants**/Children/Adolescents‡ 0-19 years	3 X 5 mcg†
Adolescents‡ 11-15 years of age	2 X 10 mcg†
Adults ≥ 20 years	3 X 10 mcg†

\*\* Infants born of HBsAg negative mothers.

† The appropriate dosage can be achieved from another formulation provided that the total volume of vaccine administered does not exceed 1.0 mL. (See text above regarding the use of the formulations without preservative).

However the 40 mcg/1.0 mL formulation can be used only for adult predialysis/dialysis patients.

‡ Adolescents (11 to 15 years of age) may receive either the 3 X 5 mcg or the 2 X 10 mcg regimen.

### Dosage Regimen for Infants Born To HBsAg Positive Mothers

Infants born to HBsAg positive mothers are at high risk of becoming chronic carriers of hepatitis B virus and of developing the chronic sequelae of hepatitis B virus infection. Well-controlled studies have shown that administration of three 0.5 mL doses of hepatitis B immune globulin starting at birth is 75% effective in preventing establishment of the chronic carrier state in these infants during the first year of life. Protection is transient under these circumstances and the effectiveness of the passively administered hepatitis B immune globulin declines thereafter. Results from clinical studies indicate that administration of one 0.5 mL dose of hepatitis B immune globulin at birth and three 5 mcg (0.5 mL) doses of HBvaxPRO, the first dose given within one week after birth, was 96% effective in preventing establishment of the chronic carrier state in infants born to HBsAg and HBeAg positive mothers. Testing for HBsAg and anti-HBs is recommended at 12-15 months to monitor the final success or failure of therapy. If HBsAg is not detectable, and anti-HBs is present, the child has been protected.

The recommended dosage for infants born to HBsAg positive mothers is as follows:

TREATMENT	BIRTH	1 MONTH	6 MONTHS
HBvaxPRO	5 mcg***	5 mcg	5 mcg
Hepatitis B immune globulin	0.5 mL	--	--

\*\*\* The first dose of **HBvaxPRO** may be given at birth at the same time as hepatitis B immune globulin but it should be administered in the opposite anterolateral thigh.

### Dosage Regimen for Infants of Mothers of Unknown HBsAg Status

In the event that a mother's HBsAg status is unknown, vaccination should be initiated as soon as possible with a 5 mcg dose of vaccine. If within 7 days of delivery, the mother is determined

to be HBsAg-positive, the infant also should be given a dose of hepatitis B immune globulin immediately; the vaccination series should then be completed with 5 mcg dosages. If the mother's HBsAg antigen test is negative, then complete the vaccination series with 5 mcg dosages.

### **Predialysis/Dialysis Regimen**

The recommended three dose vaccination regimen for predialysis/dialysis patients is as follows:

<b>GROUP</b>	<b>INITIAL</b>	<b>1 MONTH</b>	<b>6 MONTHS</b>
Adult Predialysis and Dialysis Patients***	40 mcg	40 mcg	40 mcg

\*\*\*Including dialysis and predialysis immunocompromised patients.

Note: There is no data available as yet on immunocompromised patients who are not also dialysis or predialysis patients.

A booster dose or revaccination with HBvaxPRO may be considered in predialysis/dialysis patients if the anti-HB level is less than 10 mIU/mL 1 to 2 months after the third dose.

The need for booster doses of vaccine should be assessed by annual antibody testing, and a booster dose given when antibody levels decline to less than 10 mIU/mL.

### **Revaccination of Nonresponders**

When persons who do not respond (anti-HBs < 10 mIU/mL) 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 two or three-dose series are administered, revaccination following completion of the primary series is not routinely recommended. Revaccination should only be considered for high-risk individuals, after weighing the benefits of vaccination against the potential risk of experiencing increased local or systemic adverse reactions.

### **Known or Presumed Exposure to HBsAg**

There are no prospective studies directly testing the efficacy of a combination of hepatitis B immune globulin and HBvaxPRO in preventing clinical hepatitis B following percutaneous, ocular or mucous membrane exposure to hepatitis B virus. Since most persons with such exposures (e.g. health care workers) are candidates for the hepatitis B vaccine and since combined hepatitis B immune globulin plus vaccine is more efficacious than hepatitis B immune globulin alone in perinatal exposures, the following guidelines are recommended for persons who have been exposed to hepatitis B virus such as through (1) percutaneous (needlestick), ocular, mucous membrane exposure to blood known or presumed to contain HBsAg, (2) human bites by known or presumed HBsAg carriers, that penetrate the skin, or (3) following intimate sexual contact with known or presumed HBsAg carriers:

Hepatitis B immune globulin (0.06 mL/kg) should be given as soon as possible after exposure and within 24 hours if possible. Hepatitis B vaccine with the age appropriate dose (10 mcg for adults) should be given intramuscularly within 7 days of exposure and second and third doses given one and six months, respectively, after the first dose.

### **Revaccination**

The duration of protective effect of HBvaxPRO in healthy vaccinees is unknown at present and the need for booster doses is not yet defined.

## **Method of administration**

### Do not inject intravenously or intradermally.

HBvaxPRO is for intramuscular injection. The deltoid muscle is the preferred site for intramuscular injection in adults. The anterolateral thigh is the recommended site for intramuscular injection in infants and young children. Data suggest that injections given in the buttocks frequently are given into fatty tissue instead of into muscle. Such injections have resulted in a lower seroconversion rate than is expected.

HBvaxPRO may be administered subcutaneously to persons at risk of haemorrhage following intramuscular injections. However, when other aluminium-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions including subcutaneous nodules has been observed. Therefore, subcutaneous administration should be used only in persons (e.g. haemophiliacs) at risk of haemorrhage following intramuscular injections.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis and other infectious agents from one person to another.

For Syringe Use Only: Withdraw the recommended dose from the vial using a sterile needle and syringe free of preservatives, antiseptics and detergents.

Shake well before withdrawal and use. Thorough agitation at the time of administration is necessary to maintain suspension of the vaccine.

The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.

NOTE: As the formulations available in New Zealand do not contain preservative: Once the single-dose vial has been penetrated, the withdrawn vaccine should be used promptly, and the vial must be discarded.

Parenteral medicine products should be inspected visually for particulate matter and discolouration prior to administration. After thorough agitation, HBvaxPRO is a slightly opaque, white suspension.

## **4.3 Contraindications**

Hypersensitivity to yeast or any other component of the vaccine.

## **4.4 Special warnings and precautions for use**

### **General**

Persons with immunodeficiency or those receiving immunosuppressive therapy require larger vaccine doses and respond less well than healthy individuals.

Because of the long incubation period for hepatitis B, it is possible for unrecognised infection to be present at the time HBvaxPRO is given. HBvaxPRO may not prevent hepatitis B in such patients.

Patients who develop symptoms suggestive of hypersensitivity after an injection should not receive further injections of HBvaxPRO (see Section 4.3 Contraindications).

Use caution when vaccinating latex-sensitive individuals since the vial stopper contains dry natural latex rubber that may cause allergic reactions.

As with any parenteral vaccine, epinephrine (adrenaline) should be available for immediate use should an anaphylactoid reaction occur.

Any serious active infection is reason for delaying use of HBvaxPRO, except when, in the opinion of the physician, withholding the vaccine entails a greater risk.

Caution and appropriate care should be exercised in administering HBvaxPRO to individuals with severely compromised cardiopulmonary status or to others in whom a febrile or systemic reaction could pose a significant risk.

All formulations of the vaccine are preservative-free.

### **Paediatric population**

Hepatitis B vaccine [recombinant], MSD has been shown to be usually well-tolerated and highly immunogenic in infants and children of all ages. Newborns have responded well; maternally transferred antibodies did not interfere with the active immune response to the vaccine. (See Section 4.2 Dose and method of administration for recommended paediatric dosage and recommended dosage for infants born to HBsAg positive mothers). The safety profile and effectiveness of the dialysis formulation in children have not been established.

### **Geriatric Use**

Clinical studies of HBvaxPRO used for licensure did not include sufficient numbers of subjects 65 years and older to determine whether they respond differently from younger subjects. However, in later studies of hepatitis B vaccines, it has been shown that a diminished antibody response and seroprotective levels can be expected in persons older than 60 years of age.

## **4.5 Interactions with other medicines and other forms of interactions**

### **Use With Other Vaccines**

Results from clinical studies indicate that HBvaxPRO can be administered concomitantly with DTP (Diphtheria, Tetanus and whole cell Pertussis), OPV (Oral Poliomyelitis Vaccine), M-M-R II (Measles, Mumps, and Rubella Virus Vaccine Live), Liquid PedvaxHIB (Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)) or a booster dose of DTaP (Diphtheria, Tetanus, acellular Pertussis), using separate sites and syringes for injectable vaccines. No impairment of immune response to individually tested vaccine antigens was demonstrated.

In addition, an HBsAg-containing product, COMVAX (Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) Vaccine), was given concomitantly with eIPV (enhanced Inactivated Poliovirus Vaccine) or VARIVAX (Varicella Virus Vaccine Live (Oka/Merck)), using separate sites and syringes for injectable vaccines. No impairment of immune response to these individually tested vaccine antigens was demonstrated.

## **Interchangeability of Recombinant and Plasma-Derived Hepatitis B Vaccines**

A clinical study has shown that in healthy neonates a regimen of hepatitis B vaccine can be initiated with other currently licensed hepatitis B vaccine and completed with HBvaxPRO. Both the recombinant and plasma-derived vaccines are of antigen subtype ad. The known amino acid sequence of the recombinant derived vaccine cannot be compared precisely to that of the plasma derived vaccine, since the latter represents a pool of antigen from several different plasma donors and has not been sequenced.

The yeast derived recombinant vaccine contains less than 1% normal yeast protein as an impurity.

### **4.6 Fertility, pregnancy and lactation**

#### **Pregnancy**

There are no well-controlled studies in pregnant women. HBvaxPRO should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

#### **Breast-feeding**

It is not known whether HBvaxPRO is excreted in human milk. Because many medicines are excreted in human milk, caution should be exercised when the vaccine is administered to nursing mothers. However, studies with hepatitis B vaccine [recombinant], MSD in 12 lactating women have failed to reveal evidence of this vaccine being excreted.

#### **Fertility**

HBvaxPRO has not been evaluated for its potential to impair fertility.

### **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**

Hepatitis B vaccine [recombinant], MSD is generally well tolerated. No adverse experiences were reported during clinical trials which could be related to the titres of antibodies to yeast. As with any vaccine, there is the possibility that broad use of the vaccine could reveal rare adverse reactions not observed in clinical trials.

In a group of studies worldwide, 3,258 doses of 10 mcg of hepatitis B vaccine [recombinant], MSD were administered to 1,252 healthy adults. Vaccine recipients were monitored for five days after each dose and the following adverse effects were reported: (similar adverse effects can be expected with 2.5 mcg and 5 mcg doses):

#### **Incidence Equal or Greater Than 1% of Injection**

*Local Reactions At Injection Site:* Injection site reactions, consisting principally of local pain, soreness and tenderness and including pruritus, erythema, ecchymoses, swelling, warmth and nodule formation.

*Body As A Whole:* Fatigue/asthenia, malaise, fever ( $\geq 100^{\circ}\text{F}$ )

*Digestive System:* Nausea, diarrhoea

*Nervous System:* Headache

*Respiratory System:* Pharyngitis, upper respiratory infection (NOS)

### **Incidence Less Than 1% of Injections**

*Body As A Whole:* Sweating, chills, flushing, aching, sensation of warmth

*Integumentary System:* Pruritus, rash, urticaria, angioedema

*Digestive System:* Vomiting, abdominal pains/cramps, dyspepsia, diminished appetite

*Musculoskeletal System:* Myalgia, arthralgia, back pain, neck pain, shoulder pain, neck stiffness

*Nervous System:* Light headedness, vertigo/dizziness, paresthesia

*Respiratory System:* Rhinitis, cough, influenza

*Special Senses:* Earache

*Haemic/lymphatic System:* Lymphadenopathy

*Psychiatric/behavioural:* Insomnia/disturbed sleep

*Urogenital System:* Dysuria

*Cardiovascular System:* Hypotension

In a study that compared the three-dose regimen (5 mcg) with the two-dose regimen (10 mcg) of HBvaxPRO II in adolescents, the overall frequency of adverse reactions was generally similar.

In a group of studies, 1636 doses of hepatitis B vaccine [recombinant], MSD were administered to 653 healthy infants and children (up to 10 years of age) who were monitored for 5 days after each dose. Injection site reactions (including erythema and swelling) and systemic complaints were reported following 8% and 17% of the injections, respectively. The most frequently reported systemic adverse reactions ( $> 1\%$  injections), in decreasing order of frequency, were irritability, tiredness, fever ( $> 101^{\circ}\text{F}$  or  $> 38^{\circ}\text{C}$  oral equivalent), crying, diarrhoea, vomiting, diminished appetite, and insomnia.

### **Additional Adverse Effects**

The following additional adverse effects have been reported with use of the marketed vaccine; however, in many instances a causal relationship to the vaccine has not been established.

*Hypersensitivity:* Anaphylaxis and symptoms of immediate hypersensitivity reactions including oedema, dyspnoea, chest discomfort, bronchial spasm, or palpitation have been reported within the first few hours after vaccination. An apparent hypersensitivity syndrome (serum-sickness-like) of delayed onset has been reported days to weeks after vaccination, including: arthritis (usually transient), and dermatologic reactions such as erythema multiforme, ecchymoses and erythema nodosum (see Section 4.4 Special warnings and precautions for use).

*Immune System:* Vasculitis, polyarteritis nodosa

*Integumentary System:* Alopecia, eczema

*Musculoskeletal System:* Arthritis, pain in extremity

*Nervous System:* Peripheral neuropathy including Bell's Palsy; Guillain-Barré syndrome, exacerbation of multiple sclerosis, multiple sclerosis, optic neuritis, seizure, febrile seizure, encephalitis, vasovagal syncope

*Special Senses:* Tinnitus, uveitis

*Haematologic:* Increased erythrocyte sedimentation rate, thrombocytopenia.



## Paediatric population

In a group of studies, 1636 doses of hepatitis B vaccine [recombinant], MSD were administered to 653 healthy infants and children (up to 10 years of age) who were monitored for 5 days after each dose. Injection site reactions (including erythema and swelling) and systemic complaints were reported following 8% and 17% of the injections, respectively. The most frequently reported systemic adverse reactions (> 1% injections), in decreasing order of frequency, were irritability, tiredness, fever (> 101°F or > 38°C oral equivalent), crying, diarrhoea, vomiting, diminished appetite, and insomnia.

## Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions at <https://nzphvc.otago.ac.nz/reporting/>.

## 4.9 Overdose

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

# 5 PHARMACOLOGICAL PROPERTIES

## Description

HBvaxPRO (hepatitis B vaccine (recombinant), MSD) is a non-infectious sub-unit viral vaccine consisting of surface antigen (HBsAg or Australia antigen) of hepatitis B virus produced in yeast cells.

A portion of the hepatitis B virus gene, coding for HBsAg, is cloned into yeast and the vaccine for hepatitis B is produced from cultures of this recombinant yeast strain according to methods developed in the Merck Research Laboratories.

The antigen is harvested and purified from fermentation cultures of a recombinant strain of the yeast *Saccharomyces cerevisiae* containing the gene for the *adw* subtype of HBsAg. The HBsAg protein is released from the yeast cells by cell disruption and purified by a series of physical and chemical methods. The currently produced vaccine contains no detectable yeast DNA and less than 1% of the protein content is from yeast. The purified protein is treated in phosphate buffer with formaldehyde and then coprecipitated with alum (potassium aluminium sulphate) to form bulk vaccine adjuvanted with amorphous aluminium hydroxyphosphate sulphate (previously referred to as aluminium hydroxide). The vaccine produced by the Merck method has been shown to be comparable to the plasma-derived vaccine in terms of protective efficacy (chimpanzee and human).

The vaccine against hepatitis B, prepared from recombinant yeast cultures, is free of association with human blood or blood products.

HBvaxPRO is a sterile suspension for intramuscular injection; however, it may be administered subcutaneously to persons at risk of haemorrhage following intramuscular injections (see Section 4.2 Dose and method of administration).

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-infectives, ATC code: J07BC01.

### Mechanism of action

HBvaxPRO is a vaccine produced in yeast cells by a recombinant DNA technique which has been shown to produce antibodies to hepatitis B virus.

### Clinical efficacy and safety

Clinical studies have established that hepatitis B vaccine [recombinant], MSD, when injected into the deltoid muscle, induced protective levels of antibody in 96% of 1213 healthy adults who received the recommended three dose regimen. Antibody responses varied with age; a protective level of antibody was induced in 98% of 787 young adults 20-29 years of age, in 94% of 249 adults 30-39 years of age, and in 89% of 177 adults  $\geq$  40 years of age. Studies with hepatitis B vaccine derived from plasma have shown that a lower response rate (81%) to vaccine may be obtained if the vaccine is administered as a buttock injection.

Seroconversion rates and geometric mean antibody titres were measured 1 to 2 months after the third dose. A protective antibody (anti-HBs) level has been defined as 10 or more sample ratio units (SRU) as determined by radioimmunoassay or positive by enzyme immunoassay.

Note: 10 SRU is comparable to 10 mIU/mL of antibody.

Predialysis and haemodialysis patients responded less well to HBvaxPRO than do healthy individuals, however, vaccination of adult patients early in the course of their renal disease produces higher seroconversion rates than revaccination after dialysis has been initiated. In two studies, where 40 mcg doses of vaccine were administered in the deltoid muscle, 89% of 28 participants developed anti-HBs with 86% achieving levels  $\geq$  10 mIU/mL. However, in two other studies, in which vaccine was inappropriately administered either in the buttock or a combination of buttock and deltoid, 62% of 47 participants developed anti-HBs with 55% achieving levels of  $\geq$  10 mIU/mL.

HBvaxPRO is highly immunogenic in younger individuals. In clinical studies, 99% of 94 infants under 1 year of age born of non-carrier mothers, 96% of 46 children 1-10 years of age, and 99% of 112 adolescents 11-19 years of age developed a protective level of antibody following the recommended 3-dose regimen of vaccine.

The protective efficacy of three 5 mcg doses hepatitis B vaccine [recombinant], MSD has been demonstrated in neonates born of mothers positive for both HBsAg and HBeAg (a core-associated antigenic complex which correlates with high infectivity). In a clinical study of infants who received one dose of hepatitis B immune globulin at birth followed by the recommended 3-dose regimen of hepatitis B vaccine [recombinant], MSD, chronic infection had not occurred in 96% of 130 infants after 9 months of follow-up. The estimated efficacy in prevention of chronic hepatitis B infection was 95% as compared to the infection rate in untreated historical controls.

Significantly fewer neonates became chronically infected when given one dose of hepatitis B immune globulin at birth followed by the recommended three dose regimen of hepatitis B vaccine [recombinant], MSD when compared to historical controls who received only a single dose of hepatitis B immune globulin. Testing for HBsAg and anti-HBs is recommended at 12-

15 months of age. If HBsAg is not detectable, and anti-HBs is present, the child has been protected.

As demonstrated in the above study hepatitis B immune globulin, when administered simultaneously with hepatitis B vaccine [recombinant], MSD at separate body sites, did not interfere with the induction of protective antibodies against hepatitis B virus elicited by the three dose vaccine.

The duration of the protective effect of hepatitis B vaccine [recombinant], MSD in healthy vaccinees is unknown at present, and the need for booster doses is not yet defined. However, long-term follow-up (5 to 9 years) of approximately 3000 high-risk vaccinees (infants of carrier mothers, male homosexuals, Alaskan Natives) who developed an anti-HBs titre of  $\geq 10$  mIU/mL when given a similar plasma-derived vaccine at intervals of 0, 1, and 6 months showed that no subjects developed clinically apparent hepatitis B infection and that 5 subjects developed antigenaemia, even though up to half of the subjects failed to maintain a titre at this level.

Persistence of vaccine-induced immunologic memory among healthy vaccinees who responded to a primary course of plasma-derived or recombinant hepatitis B vaccine has been demonstrated by an anamnestic antibody response to a booster dose of hepatitis B vaccine [recombinant], MSD given 5-12 years later. Data from a follow-up study showed that a group of adolescents and adults immunised 13 years earlier with a primary series of hepatitis B vaccine [recombinant], MSD, including several individuals whose antibody level had subsequently fallen below 10 mIU/mL, retained immunologic memory and were able to mount a vigorous secondary antibody response to a booster dose of hepatitis B vaccine [recombinant], MSD. A booster dose or revaccination with the dialysis formulation may be considered in predialysis/dialysis patients if the anti-HBs level is less than 10 mIU/mL 1 to 2 months after the third dose.

Reports in the literature describe a more virulent form of hepatitis B associated with superinfections or co-infections by delta virus, an incomplete RNA virus. Delta virus can only infect and cause illness in persons infected with hepatitis B virus since the delta agent requires a coat of HBsAg in order to become infectious. Therefore, persons immune to hepatitis B virus infection should also be immune to delta virus infection.

## **5.2 Pharmacokinetic properties**

Not Applicable

## **5.3 Preclinical safety data**

Animal reproduction studies have not been conducted with HBvaxPRO.

# **6 PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Sodium borate  
Sodium chloride  
Water for injection

Adjuvant

aluminum provided as amorphous aluminum hydroxyphosphate sulfate

## 6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

## 6.3 Shelf life

3 years

## 6.4 Special precautions for storage

Store unopened and opened vials at 2-8°C (35.6-46.4°F). Do not freeze since freezing destroys potency. Protect from light. Storage above or below the recommended temperature may reduce potency.

HBvaxPRO should be administered as soon as possible after being removed from refrigeration. HBvaxPRO can be administered provided total (cumulative multiple excursion) time out of refrigeration (at temperatures between 8°C and 25°C) does not exceed 72 hours. Cumulative multiple excursions between 0°C and 2°C are also permitted as long as the total time between 0°C and 2°C does not exceed 72 hours. These are not, however, recommendations for storage.

NOTE: As the formulations available in New Zealand do not contain preservative: Once the single-dose vial has been penetrated, the withdrawn vaccine should be used promptly, and the vial must be discarded.

## 6.5 Nature and contents of container

HBvaxPRO is supplied as:

- 1 mL single dose vial containing 10 mcg hepatitis B surface antigen per vial (without preservative).
- 0.5 mL single dose vial containing 5 mcg of hepatitis B surface antigen per vial (without preservative).
- 1 mL single dose vial containing 40 mcg hepatitis B surface antigen per vial (dialysis formulation (without preservative)).

## 6.6 Special precautions for disposal and other handling

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

## 7 MEDICINE SCHEDULE

Prescription Medicine

## 8 SPONSOR

Merck Sharp & Dohme (New Zealand) Ltd  
P O Box 99 851  
Newmarket  
Auckland 1149  
NEW ZEALAND  
Tel: 0800 500 673

## **9 DATE OF FIRST APPROVAL**

15 October 1987

## **10 DATE OF REVISION OF THE TEXT**

31 May 2019

### **SUMMARY TABLE OF CHANGES**

Section Changed	Summary of new information
All sections	Data Sheet reformat
6.4	Added "Protect from light" and included text for time out of refrigeration