ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Tritanrix-HB®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Tritanrix-HB® contains diphtheria (D), tetanus (T) toxoids, inactivated pertussis bacteria (Pw) and the purified major surface antigen of the hepatitis B virus (HBV), adsorbed on aluminium salts.

The D and T toxoids are prepared from the toxins of cultures of *Corynebacterium diphtheriae* and *Clostridium tetani* by formalin inactivation using established technology. The Pw component is obtained by heat inactivation of phase I culture of *Bordetella pertussis* bacteria.

The surface antigen of the HBV (HBsAg) is produced by culture of genetically-engineered yeast cells *(Saccharomyces cerevisiae)* which carry the gene coding for the major surface antigen of the HBV. This HBsAg expressed in yeast cells is purified by several physico-chemical steps. The HBsAg assembles spontaneously, in the absence of chemical treatment, into spherical particles of 20 nm in average diameter containing non-glycosylated HBsAg polypeptide and a lipid matrix consisting mainly of phospholipids. Extensive tests have demonstrated that these particles display the characteristic properties of the natural HBsAg.

A 0.5 ml dose of vaccine contains not less than 30 IU of adsorbed D toxoid, not less than 60 IU of adsorbed T toxoid, not less than 4 IU of Pw, and 10 µg of recombinant HBsAg protein.

3. PHARMACEUTICAL FORM

Suspension for intramuscular injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Tritanrix-HB® is indicated for active immunisation against diphtheria, tetanus, pertussis and hepatitis B (HB) in infants from 6 weeks onwards (see **Posology**).

4.2. Posology and method of administration

Posology

The recommended dose (0.5 ml) of the vaccine must be administered.

The primary vaccination schedule consists of three doses within the first six months of life. Where HB vaccine is not given at birth, the combined vaccine can be administered beginning as early as 8 weeks of age. Where there is a high endemicity of HB, the practice to administer HB vaccine at birth should be continued. In these circumstances, vaccination with the combined vaccine should start at 6 weeks of age.

Three vaccine doses must be administered at intervals of at least 4 weeks.

In the case of children born of known HB carrier mothers the immunoprophylactic measures for hepatitis B should not be modified. This may require separate vaccination with HB and DTPw vaccines and also include the administration of HBIg at birth.

At this point in time, insufficient data are available to support the recommendation of a booster dose of the combined vaccine. The administration of a booster dose with DTP vaccine is recommended before the end of the second year of life. For longterm protection, a booster dose of HB vaccine could also be administered after the first year of life. However, the need for this dose is currently not established.

Method of administration

Tritanrix-HB® is for deep intramuscular injection, preferably in the anterolateral thigh.

It is recommended that in patients with thrombocytopenia or bleeding disorders the vaccine be administered subcutaneously (see **4.4.**).

4.3. Contra-indications

Tritanrix-HB® should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus, pertussis or HB vaccines.

As with other vaccines, the administration of Tritanrix-HB® should be postponed in subjects suffering from acute severe febrile illness.

Tritanrix-HB® is contra-indicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances the vaccination course should be continued with DT and HB vaccines.

4.4. Special warnings and special precautions for use

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

If any of the following events occur in temporal relation to receipt of Tritanrix-HB®, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered.

Temperature of $\geq$ 40 ^{0}C within 48 hours, not due to another identifiable cause.

Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.

Persistent crying lasting $\geq$ 3 hours, occurring within 48 hours.

Convulsions with or without fever, occurring within 3 days.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

A history of febrile convulsions, a family history of convulsions, a family history of SIDS (Sudden Infant Death Syndrome) and a family history of an adverse event following Tritanrix-HB® vaccination do not constitute contra-indications.

As stated in section 4.2, there are insufficient data to support the use of Tritanrix-HB® after the first year of life.

HIV infection is not considered as a contra-indication for diphtheria, tetanus, pertussis and HB vaccination. The expected immunological response may not be obtained after vaccination of immunosuppressed patients, eg. patients on immunosuppressive therapy.

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccinee should remain under medical supervision for 30 minutes after vaccination.

Tritanrix-HB® should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

TRITANRIX-HB® SHOULD UNDER NO CIRCUMSTANCES BE ADMINISTERED INTRAVENOUSLY.

4.5. Interaction with other medicaments and other forms of interaction

It is current practice in paediatric vaccination to co-administer different vaccines during the same session with injectable vaccines being administered at separate injection sites.

Tritanrix-HB® can be administered simultaneously at separate sites or in any temporal relationship with other paediatric vaccines if this fits conveniently in the immunisation scheme.

In clinical studies, Tritanrix-HB® has been administered simultaneously with oral polio vaccine (OPV) and *Haemophilus influenzae* type b (Hib) vaccine. In these studies the immune response to the oral polio vaccine has not been investigated, however, previous experience with simultaneous administration of DTP, OPV and HB vaccines has not shown any interference. In one clinical study, Tritanrix-HB® was used to reconstitute the lyophilised Hib vaccine (Hiberix™); no interference in the immune response to any of the antigens was observed as compared to the responses observed following administration of the vaccines at separate sites. (see **6.2**.)

In patients receiving immunosuppressive therapy or patients with immunodeficiency, an adequate response may not be achieved.

4.6. Pregnancy and lactation

As Tritanrix-HB® is not intended for use in adults, information on the safety of the vaccine when used during pregnancy or lactation is not available.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

In clinical studies, local signs and symptoms were solicited, and redness (> 2 cm) and swelling (> 2 cm) occurring within 48 hours were reported with a frequency of 5.0% and 9.2% of administered

doses respectively. Parents/guardians observed severe tenderness at the site of injection in 3.2% of the doses administered.

The following general events unusual crying, drowsiness, irritability, gastrointestinal symptoms and feeding problems were also solicited. These events were reported within 48 hours and in less than 5.0% of the doses administered these were considered as severe. Fever was recorded in 40%, but in only 0.6% of the doses administered was a temperature of more than 39.5°C noted.

These events lasted only for a few days.
During the entire study period the following general events were reported with a frequency of less than 3%: pharyngitis, pneumonia, respiratory disorder, bronchitis, otitis media. These events were considered intercurrent diseases and not related to the administration of the Tritanrix-HB® vaccine.

In a prospective comparative study, which compared the administration of the combined DTPw HB vaccine with the simultaneous separate administration of DTPw and HB vaccine, higher incidences of pain, redness, swelling and fever were reported in the group receiving the combined vaccine. The incidences are presented below :

	Group 1	**Group 2**	
	DTPw HB (combined)	**DTPw (separate)**	**HB (separate)**
N° of symptom checklists	*175*	*177*	*177*
Local symptoms (%)			
Pain Total	32.0	15.3	2.8
Severe*	0.0	0.0	0.0
Redness Total	38.9	27.1	5.1
> 2cm	9.1	3.4	0.6
Swelling Total	30.9	21.5	4.5
> 2cm	10.9	3.4	0.6
General Symptoms (%)			
Fever ≥ 38°C	53.1	35.0	
Fever > 39.5°C	1.1	0.0	

* reported by the parents as adversely affecting the child's daily activities

For both vaccination groups, the majority of the reactions were short lasting.

4.9. Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code JO7CA.

Three different schedules have been studied (2-4-6 months; 3-4-5 months and 3-41/2-6 months) according to routine vaccination practices in different countries with three doses administered within the first six months of life.
For the four components of the vaccine the following immune responses, have been documented one month after completion of the primary vaccination schedule.

Anti-diphtheria antibodies
99.7% of subjects developed protective antibody titers.

Anti-tetanus antibodies
100% of subjects developed protective antibody titers.

Anti-*B pertussis* antibodies
97.7% of subjects were considered to have responded to the vaccine.

Anti-HBs antibodies
99.2% of subjects developed protective antibody titers of $\geq$ 10 mIU/ml.

5.2. Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Aluminium hydroxide, aluminium phosphate, 2-phenoxyethanol, polysorbate 20, sodium chloride, thiomersal and water for injection.

6.2. Incompatibilities

The vaccine should not be mixed with other vaccines in the same syringe with the exception of the lyophilised Hib vaccine (Hiberix™) (see **4.5.**).

6.3. Shelf-life

The expiry date of the vaccine is indicated on the label and packaging.
When stored under prescribed conditions of temperatures between +2°C and +8°C, the shelf-life is 24 months.

6.4. Special precautions for storage

Tritanrix-HB® should be stored at +2°C to +8°C.
Do not freeze. Discard if the vaccine has been frozen.

Keep out of reach of children.

6.5. Nature and contents of container

Tritanrix-HB® is presented as a suspension in a monodose glass vial.
Upon storage, a white deposit and clear supernatant can be observed.

The vials are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

6.6. Instructions for use/handling

The vaccine should be well shaken in order to obtain a homogeneous turbid white suspension and visually inspected for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

7. MARKETING AUTHORISATION HOLDER

SmithKline Beecham Biologicals S.A.
rue de l'Institut 89
1330 Rixensart, Belgium
Telephone: +32 (0)2 656 8111
Fax: +32 (0)2 656 8000
Telex: 63251 SB BIO B

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

10. DATE OF REVISION OF THE TEXT

1. NAME OF THE MEDICINAL PRODUCT

Tritanrix-HB®

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The D and T toxoids are prepared from the toxins of cultures of *Corynebacterium diphtheriae* and *Clostridium tetani* by formalin inactivation using established technology. The Pw component is obtained by heat inactivation of phase I culture of *Bordetella pertussis* bacteria.

The surface antigen of the HBV (HBsAg) is produced by culture of genetically-engineered yeast cells *(Saccharomyces cerevisiae)* which carry the gene coding for the major surface antigen of the HBV. This HBsAg expressed in yeast cells is purified by several physico-chemical steps. The HBsAg assembles spontaneously, in the absence of chemical treatment, into spherical particles of 20 nm in average diameter containing non-glycosylated HBsAg polypeptide and a lipid matrix consisting mainly of phospholipids. Extensive tests have demonstrated that these particles display the characteristic properties of the natural HBsAg.

A 0.5 ml dose of vaccine contains not less than 30 IU of adsorbed D toxoid, not less than 60 IU of adsorbed T toxoid, not less than 4 IU of Pw, and 10 µg of recombinant HBsAg protein.

3. PHARMACEUTICAL FORM

Suspension for intramuscular injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Tritanrix-HB® is indicated for active immunisation against diphtheria, tetanus, pertussis and hepatitis B (HB) in infants from 6 weeks onwards (see **Posology**).

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At this point in time, insufficient data are available to support the recommendation of a booster dose of the combined vaccine. The administration of a booster dose with DTP vaccine is recommended before the end of the second year of life. For longterm protection, a booster dose of HB vaccine could also be administered after the first year of life. However, the need for this dose is currently not established.

Method of administration

Tritanrix-HB® is for deep intramuscular injection, preferably in the anterolateral thigh.

It is recommended that in patients with thrombocytopenia or bleeding disorders the vaccine be administered subcutaneously (see **4.4.**).

4.3. Contra-indications

Tritanrix-HB® should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus, pertussis or HB vaccines.

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Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

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Temperature of $\geq$ 40 ^{0}C within 48 hours, not due to another identifiable cause.

Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.

Persistent crying lasting $\geq$ 3 hours, occurring within 48 hours.

Convulsions with or without fever, occurring within 3 days.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

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4.6. Pregnancy and lactation

As Tritanrix-HB® is not intended for use in adults, information on the safety of the vaccine when used during pregnancy or lactation is not available.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

In clinical studies, local signs and symptoms were solicited, and redness (> 2 cm) and swelling (> 2 cm) occurring within 48 hours were reported with a frequency of 5.0% and 9.2% of administered doses respectively. Parents/guardians observed severe tenderness at the site of injection in 3.2% of the doses administered.

The following general events unusual crying, drowsiness, irritability, gastrointestinal symptoms and feeding problems were also solicited. These events were reported within 48 hours and in less than 5.0% of the doses administered these were considered as severe. Fever was recorded in 40%, but in only 0.6% of the doses administered was a temperature of more than 39.5°C noted.

These events lasted only for a few days.

During the entire study period the following general events were reported with a frequency of less than 3%: pharyngitis, pneumonia, respiratory disorder, bronchitis, otitis media. These events were considered intercurrent diseases and not related to the administration of the Tritanrix-HB® vaccine.

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Local symptoms (%)			
Pain Total	32.0	15.3	2.8
Severe*	0.0	0.0	0.0
Redness Total	38.9	27.1	5.1
> 2cm	9.1	3.4	0.6
Swelling Total	30.9	21.5	4.5
> 2cm	10.9	3.4	0.6
General Symptoms (%)			
Fever ≥ 38°C	53.1	35.0	
Fever > 39.5°C	1.1	0.0	

* reported by the parents as adversely affecting the child's daily activities

For both vaccination groups, the majority of the reactions were short lasting.

4.9. Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code JO7CA.

Three different schedules have been studied (2-4-6 months; 3-4-5 months and 3-4.1/2-6 months) according to routine vaccination practices in different countries with three doses administered within the first six months of life.
For the four components of the vaccine the following immune responses, have been documented one month after completion of the primary vaccination schedule.

Anti-diphtheria antibodies
99.7% of subjects developed protective antibody titers.

Anti-tetanus antibodies
100% of subjects developed protective antibody titers.

Anti-*B pertussis* antibodies
97.7% of subjects were considered to have responded to the vaccine.

Anti-HBs antibodies
99.2% of subjects developed protective antibody titers of $\geq$ 10 mIU/ml.

5.2. Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Aluminium hydroxide, aluminium phosphate, 2-phenoxyethanol, polysorbate 20, sodium chloride, thiomersal and water for injection.

6.2. Incompatibilities

The vaccine should not be mixed with other vaccines in the same syringe with the exception of the lyophilised Hib vaccine (Hiberix™) (see **4.5.**).

6.3. Shelf-life

The expiry date of the vaccine is indicated on the label and packaging.
When stored under prescribed conditions of temperatures between +2°C and +8°C, the shelf-life is 24 months.

6.4. Special precautions for storage

Tritanrix-HB® should be stored at +2°C to +8°C.
Multidose vials should be stored at +2°C to +8°C throughout their use.
Do not freeze. Discard if the vaccine has been frozen.

Keep out of reach of children.

6.5. Nature and contents of container

Tritanrix-HB® is presented as a suspension in a multidose glass vial.
Upon storage, a white deposit and clear supernatant can be observed.

The vials are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

6.6. Instructions for use/handling

The vaccine should be well shaken in order to obtain a homogeneous turbid white suspension and visually inspected for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

When using a multidose vial, each dose should be taken with a strerile needle and syringe. As with other vaccines, a dose of vaccine should be withdrawn under strict aseptic conditions and precautions taken to avoid contamination of the contents.

7. MARKETING AUTHORISATION HOLDER

SmithKline Beecham Biologicals S.A.
rue de l'Institut 89
1330 Rixensart, Belgium
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Fax: +32 (0)2 656 8000
Telex: 63251 SB BIO B

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

10. DATE OF REVISION OF THE TEXT

ANNEX II
MANUFACTURING AUTHORISATION AND CONDITIONS OF THE MARKETING AUTHORISATION

A. HOLDER(S) OF THE MANUFACTURING AUTHORISATION(S)

Manufacturer of the active substance:

For Diphtheria toxoid, tetanus toxoid and inactivated Bordetella pertussis;
Behringwerke AG, Postfach 1140, 3550 Marburg/Lahn, Germany.

For Hepatitis B surface antigen (HBsAg);
SmithKline Beecham Biologicals, 89, rue de l'Institut, 1330 Rixensart, Belgium.

Manufacturer of the finished medicinal product and responsible for batch release in the European Economic Area:

SmithKline Beecham Biologicals, 89, rue de l'Institut, 1330 Rixensart, Belgium.

Manufacturing authorisation issued on 18 April 1995, to SmithKline Beecham Biologicals S. A, by the Ministry of Public Health and Environment (Ministère de la Santé Publique et de l'Environnement/Ministerie van Volksgezondheid en Leefmilieu) Vesaliusgebouw, Riksadministratief centrum, 1010 Brussels.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal Product subject to renewable medical prescription

C. SPECIFIC OBLIGATIONS OF THE MARKETING AUTHORISATION HOLDER

The company, after having been consulted (letter from SmithKline Beecham Biologicals dated 11 March 1996) agreed to fulfil the commitment to submit within the defined time-frame, to the EMEA, the information requested by the CPMP.

Pharmacovigilance:

In addition to the post marketing surveillance as foreseen in council Regulation 2309/93, the company has made a committment to initiate additional surveillance outside the EU in consultation with the involved authorities. A progress report on this matter will be submitted to the EMEA 12 months after the marketing authorisation is granted.

SPC commitment:

The company commits, upon issuance of a marketing authorisation for their combined diptheria, tetanus, acellular pertussis, hepatitis B vaccine, to modify the SPC/PIL for Tritanrix-HB®. This modification will reflect the identified benefits of the combination with acellular pertussis as compared to the combination with whole-cell pertussis.

ANNEX III
LABELLING AND USER PACKAGE LEAFLET

A- LABELLING

Carton - Monodose Vial Text

DTPw-HB vial pack

p.1
Tritanrix-HB®
Combined diphtheria, tetanus, whole-cell pertussis and hepatitis B vaccine
1 dose = 0.5 ml
Suspension for injection; intramuscular use
SMITHKLINE BEECHAM BIOLOGICALS

p.2
Tritanrix-HB®
1 dose (0.5 ml) contains

Diphtheria toxoid	min. 30 IU
Tetanus toxoid	min. 60 IU
Inactivated whole-cell Bordetella pertussis	min. 4 IU
HBsAg Purified	10 µg
Al^{+++}	0.63 mg
Thiomersal	25 µg
2-phenoxyethanol	0.5 mg
Sodium chloride	4.5 mg
Polysorbate 20	max 5 µg
Water for injections	up to 0.5 ml

Storage : +2°C/+8°C
Do not freeze

p.3
Tritanrix-HB®
Combined diphtheria, tetanus, whole-cell pertussis and hepatitis B vaccine
1 dose = 0.5 ml
Suspension for injection; intramuscular use
SMITHKLINE BEECHAM BIOLOGICALS
rue de l'Institut, 89
1330 Rixensart, Belgium

p.4
SmithKline Beecham Biologicals s.a.
Rixensart, Belgium
Keep out of reach of children

Medicinal product subject to medical prescription

p.5
Tritanrix-HB®
Combined vaccine DTPw-HB
1 dose (0.5 ml)

p.6
Tritanrix-HB®
MANUFACTURER'S BATCH NUMBER:
EXPIRY DATE: (MONTH/YEAR)
AUTHORIZATION No:
Label : Monodose Vial

Vial label
Tritanrix-HB®
Combined vaccine DTPw-HB
1 dose = 0.5 ml
Suspension for injection; intramuscular use
Storage : +2°C/+8°C
Do not freeze
SB Biologicals - Rixensart - Belgium
MANUFACTURER'S BATCH NUMBER:
EXPIRY DATE: (MONTH/YEAR)

Carton - Multidose Vial Text

DTPw-HB vial pack

p.1
Tritanrix-HB®
10 doses
Combined diphtheria, tetanus, whole-cell pertussis and hepatitis B vaccine
1 dose = 0.5 ml
Suspension for injection; intramuscular use
SMITHKLINE BEECHAM BIOLOGICALS

p.2
Tritanrix-HB®
10 doses
1 dose (0.5 ml) contains

Diphtheria toxoid	min. 30 IU
Tetanus toxoid	min. 60 IU
Inactivated whole-cell Bordetella pertussis	min. 4 IU
HBsAg Purified	10 µg
Al^{+++}	0.63 mg
Thiomersal	25 µg
2-phenoxyethanol	0.5 mg
Sodium chloride	4.5 mg
Polysorbate 20	max 5 µg
Water for injections	up to 0.5 ml

Storage : +2°C/+8°C
Do not freeze

p.3
Tritanrix-HB®
10 doses
Combined diphtheria, tetanus, whole-cell pertussis and hepatitis B vaccine
1 dose = 0.5 ml
Suspension for injection; intramuscular use
SMITHKLINE BEECHAM BIOLOGICALS
rue de l'Institut, 89
1330 Rixensart, Belgium

p.4
SmithKline Beecham Biologicals s.a.
Rixensart, Belgium
Keep out of reach of children

Medicinal product subject to medical prescription

p.5
Tritanrix-HB®
10 doses
Combined vaccine DTPw-HB
1 dose (0.5 ml)

p.6
Tritanrix-HB®
MANUFACTURER'S BATCH NUMBER:
EXPIRY DATE: (MONTH/YEAR)
AUTHORIZATION No:
Label : Multidose Vial Text

Vial label
Tritanrix-HB®
10 doses
Combined vaccine DTPw-HB
1 dose = 0.5 ml
Suspension for injection; intramuscular use
Storage : +2°C/+8°C
Do not freeze
SB Biologicals - Rixensart - Belgium
MANUFACTURER'S BATCH NUMBER:
EXPIRY DATE: (MONTH/YEAR)

B- USER PACKAGE LEAFLET

What you should know about Tritanrix-HB®? 3 ml monodose vial

- Please read this leaflet carefully before your child receives the vaccine.
- Keep this leaflet until your child has finished the complete vaccination course. You may want to read it again.
- You must follow the advice of the doctor or nurse carefully. If there is anything you do not understand, please ask the doctor, nurse or pharmacist.
- Make sure your child finishes the complete vaccination course. If not, your child may not be fully protected against infection.
- Always keep vaccines out of reach of children.
- Like all vaccines, Tritanrix-HB® may occasionally cause unwanted effects. (You will find more information about this later in the leaflet.)
- The vaccine should be administered by a health care professional.

If you have any additional questions, or are not sure about anything, ask the doctor, nurse or pharmacist.

What is Tritanrix-HB®?

Tritanrix-HB® is a combined tetanus, diphtheria, pertussis (whooping cough) and hepatitis B vaccine and contains non-infectious substances from tetanus, diphtheria, pertussis bacteria and the surface protein of the hepatitis B virus (HBV) as active ingredients*)*. The surface protein of the HBV (HBsAg) is produced by culture of genetically-engineered yeast cells *(Saccharomyces cerevisiae).*

The vaccine is provided in one dose (0.5 ml) glass vial for use in infants from 6 weeks of age.

Tritanrix-HB® contains as inactive ingredients: aluminium hydroxide, aluminium phosphate, 2-phenoxyethanol, polysorbate 20, sodium chloride, thiomersal and water for injection.

Tritanrix-HB® is presented as a suspension for intramuscular injection.

Manufacturer and marketing authorisation holder *:*

SmithKline Beecham
Biologicals S.A.
rue de l'Institut 89
B-1330 Rixensart
Belgium

What does Tritanrix-HB® do?

Tritanrix-HB® protects your child against tetanus, diphtheria, pertussis and hepatitis B. It works by helping the body to make its own antibodies which protect your child against these diseases.

What should be checked before receiving the vaccine?

Your child should not receive the vaccine if you think she/he has previously had an allergic reaction to Tritanrix-HB® or any other tetanus, diphtheria, pertussis or hepatitis B vaccine.

The vaccination should be delayed if your child has an infection with a high temperature.

Tell the doctor:
- if your child has experienced any health problems after previous administration of a diphtheria, tetanus, pertussis vaccine such as:
  - temperature more than 40 °C within 48 hours of receiving the vaccination
  - collapse or shock-like state within 48 hours of receiving the vaccination
  - persistent crying lasting more than 3 hours, occurring within 48 hours of receiving the vaccination
  - convulsions, occurring within 3 days of receiving the vaccination
- if your child has any bleeding problems.
- if anyone in your family has had convulsions.
- if your child is taking any other medicine or has recently received any other vaccine.

How will the vaccine be given?

The doctor or nurse will inject the recommended dose of vaccine.

Tritanrix-HB® will be injected into your child's upper outer thigh.

If your child has any bleeding problems tell the doctor or nurse before receiving Tritanrix-HB®, as the vaccine may need to be given in a different way (under the skin).

Normally, your child should receive three doses of vaccine. Each dose will be given on separate occasions with an interval of at least 4 weeks between doses. It is important to follow the instructions from the doctor/nurse regarding return visits for the following doses. If an additional dose is necessary, the doctor will tell you.

If you forget to go back to the doctor at the scheduled time, ask the doctor for advice.

What are the possible side effects?

As with other vaccines your child may feel pain or discomfort at the injection site, or you may see some redness and swelling at this site. However, these reactions usually clear up within a few days.

Other reactions which can occur are unusual crying, fever, drowsiness, irritability, feeding problems and gastrointestinal symptoms such as vomiting, diarrhoea.
If these symptoms continue or become severe, tell the doctor or nurse.

As with all injectable vaccines, there is an extremely small risk of a severe allergic reaction. (This can be recognised by symptoms such as difficulty in breathing or swallowing, itchy rash of the hands and feet, swelling of the eyes and face). Such reactions will usually occur before leaving the doctor's office, but in any event you should seek immediate treatment.

If your child develops any other symptom within days following the vaccination, tell the doctor as soon as possible.

How to keep Tritanrix-HB®?

The expiry date is indicated on the label and packaging. The vaccine should not be used after this date.

Store your vaccine in a refrigerator between +2°C and +8°C. The vaccine should not be frozen.

Store all vaccines out of the reach of children.

Specific information for the administrator

- Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

- If any of the following events occur in temporal relation to receipt of Tritanrix-HB®, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered.

  Temperature of $\geq$ 40 °C within 48 hours, not due to another identifiable cause.

  Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.

  Persistent crying lasting $\geq$ 3 hours, occurring within 48 hours.

  Convulsions with or without fever, occurring within 3 days.

  There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

- The vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration.
  Before use of Tritanrix-HB®, the vaccine should be well shaken to obtain a homogeneous turbid suspension.
  Do not use if the content appears otherwise.

- Tritanrix-HB® is for deep intramuscular injection, preferably in the anterolateral thigh.

- Exceptionally the vaccine may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders.

- Tritanrix-HB® should not be administered intravenously.

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

- Different injectable vaccines should always be administered at different injection sites.

DATE OF APPROVAL OF UPL

What you should know about Tritanrix-HB®? 10 ml multidose vial

- Please read this leaflet carefully before your child receives the vaccine.
- Keep this leaflet until your child has finished the complete vaccination course. You may want to read it again.
- You must follow the advice of the doctor or nurse carefully. If there is anything you do not understand, please ask the doctor, nurse or pharmacist.
- Make sure your child finishes the complete vaccination course. If not, your child may not be fully protected against infection.
- Always keep vaccines out of reach of children.
- Like all vaccines, Tritanrix-HB® may occasionally cause unwanted effects. (You will find more information about this later in the leaflet.)
- The vaccine should be administered by a health care professional.

If you have any additional questions, or are not sure about anything, ask the doctor, nurse or pharmacist.

What is Tritanrix-HB®?

Tritanrix-HB® is a combined tetanus, diphtheria, pertussis (whooping cough) and hepatitis B vaccine and contains non-infectious substances from tetanus, diphtheria, pertussis bacteria and the surface protein of the hepatitis B virus (HBV) as active ingredients*)*. The surface protein of the HBV (HBsAg) is produced by culture of genetically-engineered yeast cells *(Saccharomyces cerevisiae)*.

The vaccine is provided in a 10-dose (5.0 ml) glass vial for use in infants from 6 weeks of age.

Tritanrix-HB® contains as inactive ingredients: aluminium hydroxide, aluminium phosphate, 2-phenoxyethanol, polysorbate 20, sodium chloride, thiomersal and water for injection.

Tritanrix-HB® is presented as a suspension for intramuscular injection.

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Tell the doctor:

- if your child has experienced any health problems after previous administration of a diphtheria, tetanus, pertussis vaccine such as:
  - temperature more than 40 °C within 48 hours of receiving the vaccination
  - collapse or shock-like state within 48 hours of receiving the vaccination
  - persistent crying lasting more than 3 hours, occurring within 48 hours of receiving the vaccination
  - convulsions, occurring within 3 days of receiving the vaccination
- if your child has any bleeding problems.
- if anyone in your family has had convulsions.
- if your child is taking any other medicine or has recently received any other vaccine.

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Tritanrix-HB® will be injected into your child's upper outer thigh.

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Normally, your child should receive three doses of vaccine. Each dose will be given on separate occasions with an interval of at least 4 weeks between doses. It is important to follow the instructions from the doctor/nurse regarding return visits for the following doses. If an additional dose is necessary, the doctor will tell you.

If you forget to go back to the doctor at the scheduled time, ask the doctor for advice.

What are the possible side effects?

As with other vaccines your child may feel pain or discomfort at the injection site, or you may see some redness and swelling at this site. However, these reactions usually clear up within a few days.
Other reactions which can occur are unusual crying, fever, drowsiness, irritability, feeding problems and gastrointestinal symptoms such as vomiting, diarrhoea.
If these symptoms continue or become severe, tell the doctor or nurse.

As with all injectable vaccines, there is an extremely small risk of a severe allergic reaction. (This can be recognised by symptoms such as difficulty in breathing or swallowing, itchy rash of the hands and feet, swelling of the eyes and face). Such reactions will usually occur before leaving the doctor's office, but in any event you should seek immediate treatment.

If your child develops any other symptom within days following the vaccination, tell the doctor as soon as possible.

How to keep Tritanrix-HB®?

The expiry date is indicated on the label and packaging. The vaccine should not be used after this date.

Store your vaccine in a refrigerator between +2°C and +8°C. The vaccine should not be frozen. Multidose vials should be stored between +2°C and +8°C throughout their use.

Store all vaccines out of the reach of children.

Specific information for the administrator

- Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

- If any of the following events occur in temporal relation to receipt of Tritanrix-HB®, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered.

  Temperature of $\geq$ 40 °C within 48 hours, not due to another identifiable cause.

  Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.

  Persistent crying lasting $\geq$ 3 hours, occurring within 48 hours.

  Convulsions with or without fever, occurring within 3 days.

  There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

- The vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration.
  Before use of Tritanrix-HB®, the vaccine should be well shaken to obtain a homogeneous turbid suspension.
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- Tritanrix-HB® is for deep intramuscular injection, preferably in the anterolateral thigh.

- Exceptionally the vaccine may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders.

- Tritanrix-HB® should not be administered intravenously.

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

- Different injectable vaccines should always be administered at different injection sites.

- When using a multidose vial, each dose should be taken with a sterile needle and syringe. As with other vaccines, a dose of vaccine should be withdrawn under strict aseptic conditions and precautions taken to avoid contamination of the contents.

DATE OF APPROVAL OF UPL

Other information : For any information regarding this product, please contact the local representative of the Marketing Authorisation holder :

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