SUMMARY OF PRODUCT CHARACTERISTICS/BROCHURE

A. Name of Medicine

Vecon Pediatric – Recombinant Hepatitis B Vaccine (*Saccharomyces cerevisiae*)

B. Dosage Form

Suspension for Injection

0.5 ml/dose/syringe

C. Drug Description

Vecon Pediatric – Recombinant Hepatitis B Vaccine (*Saccharomyces cerevisiae*) is a preparation made of purified hepatitis B surface antigen (HBsAg) expressed by the recombinant *Saccharomyces cerevisiae*. After purification of HBsAg, a quantity of aluminum adjuvant is added to make the vaccine. The vaccine is a milky-white suspension with stratified precipitate which can be dispersed by shaking. It contains no preservative.

D. Drug Composition

Components of formulation (per 0.5 mL of final bulk①)

Components of formula	Content	Function
Hepatitis B Surface Antigen	10 μg	Active ingredient
Sodium chloride	4.5 mg	Solvent
Potassium aluminum sulfate dodecahydrate②	1.52 mg	Adjuvant
Sodium hydroxide②	0.385 mg	Adjuvant

Note: ① Calculated as 0.5 mL of final bulk, due to the final product strength of 0.5ml/prefilled syringe.

② Potassium aluminum sulfate and sodium hydroxide are added to form Kombinasi Aluminum Hydroxide Adjuvant.

E. Indications

Vecon Pediatric can induce immunity against hepatitis B virus in recipients following immunization. It is used to prevent hepatitis B. Eligible for the subjects susceptible to hepatitis B virus, newborn and infants younger than 1 year of age, especially newborns born by Hepatitis B Surface Antigen and/or HBeAg-positive mothers.

F. Posology and Method of Administration

The immunization schedules for HepB vaccine should be based on official recommendations.

Vecon Pediatric should be injected intramuscularly. **The anterolateral aspect of the thigh is the preferred site for intramuscular injection for newborn and infants younger than 1 year of age**.

For newborns and infants younger than 1 year of age who are susceptible to the hepatitis B virus, especially newborns born by Hepatitis B Surface Antigen and/or HBeAg-positive mothers, three injections (0.5 mL each dose) for a complete immunization course at the schedule of 0, 1 and 6 months will be given. The first injection for the newborns shall be given within 24 hours after birth.

G. Direction for use

The vaccine should be shaken well to obtain a homogeneous white suspension prior to expelling air from the syringe, and should be inspected visually for any particulate matter and/or variation of physical aspect prior to administration. Do not use if there is foreign matter in the content. The vaccine shall be administered immediately after the container is opened.

H. Contraindications

(1) Subjects with known allergic reaction to any component of the vaccine, including excipients and formaldehyde.
(2) Subjects with acute diseases, severe chronic diseases, chronic diseases at acute attack stage or fever.
(3) Subjects with allergic history of Hepatitis A &B combined vaccine or Hepatitis B vaccine.
(4) Subjects with uncontrolled epilepsy or other progressive diseases of nervous system.

I. Warnings and Precautions

Precautions

(1) Adrenaline should be available for first aid in case of severe anaphylactic reactions. The recipients shall be observed for at least 30 minutes on site following injection.
(2) The vaccine shall be administered with caution to the subjects with family or individual history of convulsion and those with chronic diseases, history of epilepsy or allergic diathesis.
(3) Normally the subjects who had abnormal reactions such as high fever or convulsions after first vaccination should not be vaccinated for the second time. The newborns to Hepatitis B Surface Antigen and/or HBeAg-positive mothers shall follow the doctor's instructions as for whether to receive the second and third injections.
(4) Shake the vaccine container well before use. Do not use the vaccine if the container shows abnormalities, such as crack, illegible label, exceeding expiry date or turbidity.
(5) The vaccine shall be administered immediately after the container is opened.

Traceability

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

J. Drug Interactions

Concomitant administration with other vaccines: No clinical research has been conducted to study the impact of synchronized immunization (immunization of other vaccines prior to or following the immunization of this vaccine, or immunization of this vaccine in combination with other vaccines) on the immunogenicity of this vaccine. No data are available to be used for assessing the effects of simultaneous vaccination of this vaccine and any other vaccine.

Concomitant administration with immunosuppressive drugs. There are no clinical studies of concomitant administration with immunosuppressant drugs. However, the use of immunosuppressants typically lowers the immune response to the vaccination.

K. Fertility, Pregnancy and Breastfeeding

Pregnancy

There are no data from the use of Recombinant Hepatitis B vaccine (Saccharomyces cerevisiae) in pregnant women. Therefore, the use of this vaccine should be avoided during pregnancy.

Breast-feeding

It is unknown whether Recombinant Hepatitis B vaccine (Saccharomyces cerevisiae) is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. (see sections **Preclinical Safety Data**)

L. Effects on Ability to Drive and Use Machines

HepB vaccine has no or negligible influence on the ability to drive and use machines. Howerver, some of the adverse effects may temporarily affect the ability to drive or use machines.

M. Side effects

Summary of safety profile

The safety profile presented below is based on a Phase III clinical study, Phase IV clinical study, PSUR (May 2015-2020), and PSUR (May 2020 – 2022). Phase III clinical study conducted in Lianshui County, Xiangshui County, Binhai County, Funing County, Yandu District, and Chuzhou District of Jiangsu Province China with 986 subjects receiving this product. Phase IV

clinical study conducted in Gaozhou and Xinxing China with the number of subjects receiving at least one dose of vaccine is 4335 subjects.

The most commonly reported adverse reactions were pain, fever, induration, and skin mucosa, allergic reaction, nausea and vomiting, swelling, erythema, weariness & asthenia, crying, and lactation or eating disorders. These adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination.

Most other adverse reactions were uncommon and similarly reported between the study groups.

Summary table of side effects reactions

Tabulated list of adverse reactions

Adverse reactions are listed below by MedDRA system organ class and frequency:

Very common : (≥ 1/10)

Common : (≥ 1/100 to < 1/10)

Uncommon : (≥ 1/1,000 < 1/100)

Rare : (≥ 1/10,000 < 1/1,000)

Very rare : (< 1/10,000)

Adverse Reaction

System Organ Class	Frequency	Adverse Reactions
Blood and lymphatic system disorders	Rare	Thrombocytopenic purpura, thrombocytopenia,
Immune system disorder	Common	Allergic reaction
Skin and subcutaneous tissue disorder	Uncommon	Rash
Nervous system disorder	Uncommon	Convulsion
Gastrointestinal disorder	Common	Nausea & vomiting
Musculoskeletal and connective tissue disorder	Very common	Skin mucosa
General disorders and administration site conditions	Very common	Pain, fever, induration
	Common	Swelling, erythema, weariness & asthenia, crying, lactation or eating disorders

	Rare	Anorexia

Adverse events should be reported to Biofarma via Bio Care 1500810 and
Pusat Farmakovigilans/MESO Nasional Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Psikotropika, Prekursor dan Zat Aktif Badan Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext. 1079

Website: https://e-meso.pom.go.id

N. Overdose and Treatment (if applicable)

Overdose with this product is unlikely due to its presentation as a pre-filled syringe.

O. Drug Mechanisms, and/or Pharmacodynamic and/or Pharmacokinetics

Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, Hepatitis vaccines, hepatitis B, purified antigen; ATC code: J07BC01.

This HepB vaccine is prepared from purified Hepatitis B Surface Antigen expressed by the yeast Saccharomyces cerevisiae, which is subjected to fed-batch culture after the S gene carrying Hepatitis B Surface Antigen and vectors constructed by regulatory units related to S gene expression are transferred into it (the yeast). The active ingredient is Hepatitis B Surface Antigen, which can stimulate the body to produce specific immunity.

Clinical trial

In Phase III clinical trials in healthy newborns, immunogenicity of 0.5ml/dose containing 10μg of Hepatitis B Surface Antigen, was evaluated and compared with the Hep B vaccines manufactured by GlaxoSmithKline. Subjects were divided into three groups according to mother's test results of "five test items of hepatitis B": ① both HBsAg and HBeAg were positive (double-positive); ② only HBsAg was positive (single-positive), and ③ HBsAg, HBeAg, HBeAb and HBcAb were all negative. Test group were vaccinated with 10 μg/0.5 mL test vaccine, and those in the control group were vaccinated with 10 μg/0.5 mL control vaccine.

The analysis was performed with blood sample test results in Month 7 after birth in the PPS, and the results were as follows:

Protection rate of mother to child transmission: For positive groups, there was no significant difference in Protection rate of mother to child transmission between test group (98.21%) and

the control group (95.17%), and there was no significant difference between the double-positive test group (95.69%) and the control group (93.94%); in the single-positive group, the result of the test group (99.47%) was superior to that of the control group (95.81%) with significance.

Anti-HBs positive conversion rate: There was no significant difference between the test group (93.55%) and the control group (90.06%) in positive groups, and no significant difference was observed between the test group (91.26%) and the control group (89.09%) in the double-positive group; There was no significant difference between the test group (94.69%) and the control group (90.74%) in the single-positive group; in the negative group, there was no significant difference between the test group (95.01%) and the 10 μg control group (94.72%).

Post-immunization anti-HBs level: For positive groups, there was no significant difference between the test group (GMT: 587.04 mIU/mL) and the control group (GMT: 563.10 mIU/mL), and no significant difference between the test group (GMT: 491.49 mIU/mL) and the control group (GMT: 457.32 mIU/mL) was observed in the double-positive group; in the single-positive group, there was no significant difference between the test group (GMT: 639.25 mIU/mL) and the control group (GMT: 626.20 mIU/mL). In the negative group, there was no significant difference between the test group (GMT: 802.83 mIU/mL) and the 10 μg control group (GMT: 797.48 mIU/mL).

The post-immunization anti-HBs levels were grouped and compared at three levels: 10 ~ 100, 100 ~ 1000, and > 1000 (mIU/mL). There was no significant difference between the test group and the control group in positive groups (including the single-positive group and the double-positive group); In the negative group, there was no significant difference between the test group and the 10 μg control group.

FAS analysis results were completely consistent with the above conclusions obtained from the PPS.

Anti HbS antibody persistence: The anti-HBs positive conversion rate, anti-HBs level (GMT), and anti-HBs level in positive groups (the double-positive group and the single-positive group) and the negative group on the Month 12 after birth were grouped and compared at three levels: 10 ~ 100, 100 ~ 1000 and > 1000 (mIU/mL). All results were decreased compared with those on Month 7 after birth. There was no significant difference between the test group and the control group in the double-positive group and the single-positive group; there was no significant difference between the test group and the 10 μg control group in the negative group.

Phase IV study

In the phase IV clinical trial study (To observe the immune persistence and safety), a total of 701 subjects were enrolled in this study. Venous blood of the subjects was collected to obtain

serum by separation at 1 month, 1 year, and 3 years after the third vaccination injection, and quantitative detection of anti-HBs was performed by chemiluminescence to evaluate the vaccine's immune persistence, including the antibody positive rate and GMC level.

548 of the subjects finished blood collection at 1 month after the whole-course immunization. In newborns from Hepatitis B Surface Antigen-positive or Hepatitis B Surface Antigen-negative mothers, the anti-HBs positive rates were 98.89% and 99.64%, and the GMCs of the anti-HBs were 636.44 mIU/ml and 681.66 mIU/ml, respectively. A total of 212 and 203 newborns from Hepatitis B Surface Antigen-positive and Hepatitis B Surface Antigen-negative mothers had their blood collected 3 years after the whole-course immunization with anti-HBs positive rates of 88.68% and 86.21% and the GMCs of the anti-HBs of 80.49 mIU/ml and 91.18 mIU/ml, respectively. A total of 19 subjects were found to exhibit adverse reactions during the safety observation period, demonstrating a total incidence of 2.71% (19/701).

Pharmacokinetic properties

Not applicable.

P. Non-Clinical Safety Data

Single dose toxicity evaluation was performed by intramuscular injection of HepB into mice. Repeated dose toxicity evaluation was performed by intramuscular injection of HepB into cynomolgus monkeys. During the test in single and repeated dose toxicity studies, there were no reported deaths of test animals, abnormalities in clinical signs, laboratory examinations, gross pathology or hispathology. The NOAEL (No Observed Adverse Effect Level) of the test vaccine in mice was 600 micrograms/kilogram and 30 µg/kg in cynomolgus monkeys.

Q. Incompatibilities (if the product need to be reconstituted before use)

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

R. Storage

Store and ship at 2-8°C, protect from light. Freezing is strictly forbidden.
During storage, a white deposit and clear supernatant can be observed. This does not constitute a sign of deterioration.
The shelf life of the vaccine is 36 months.

S. Packaging Type and Size

Box, 1 PRE-FILLED SYRINGE (PFS) @ 10 µg/0.5 mL (1 dose).

Nature and contents of container:

1.0 ml suspension for injection in pre-filled syringe (Neutral borosilicate glass) with a plunger stopper (Chlorinated butyl rubber plunger) and protective-tip cap (Polyisoprene Rubber).

This product is filled into pre-filled syringe, 1 syringe per box.

T. Other Listed Dosage Form and Packaging (if any)

Box, 1 PRE-FILLED SYRINGE (PFS) @ 20 µg/1.0 mL (1 dose)

Box, 1 vial@ 10 µg/0.5 mL (1 dose)

U. Marketing Authorization Number

-

V. Drug Class

Prescription Drug

W. Special Warning

On Medical Prescription Only

- Do not use if there is foreign matter in the content.
- The vaccine shall be administered immediately after the container is opened.
- No special requirements for disposal.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Manufactured by.

Shenzhen Kangtai Biological Products Co., Ltd.

No. 18, Shutianpu Road, Matian Street, Guangming District, Shenzhen

Zip Code: 518106

Hotline: 4008806992

Tel: 86-755-26988686

Fax: 860755026988585

Website: www.biokangtai.com

Imported by.

PT Bio Farma (Persero)
Jl. Pasteur No. 28 – Bandung 40161 - Indonesia
PO Box 1136. Tel. +62 22 2033755
Fax. +62 22 2041306
www.biofarma.co.id

INFORMASI PRODUK UNTUK PASIEN

Vecon Pediatric® Vaksin Hepatitis B Rekombinan **Suspensi Injeksi**

Informasi Produk (PIL) ini mengandung informasi yang dapat membantu untuk mengetahui manfaat dan risiko penggunaan Vecon Pediatric® yang sudah atau akan anak Anda terima. Bicarakan kepada tenaga kesehatan yang merawat Anda apabila ada pertanyaan lebih lanjut.

Apa itu Vecon Pediatric®?
Vecon Pediatric® merupakan produk suspensi injeksi yang mengandung vaksin Hepatitis B rekombinan. Vaksin ini dapat merangsang tubuh untuk menghasilkan kekebalan dan digunakan untuk mencegah penyakit menular yang disebabkan oleh virus hepatitis B.

Terbuat dari apakah Vecon Pediatric®?
Vecon Pediatric® terbuat dari pemurnian *Hepatitis B Surface Antigen* yang diekspresikan oleh *Saccharomyces cerevisiae* rekombinan. Setelah dilakukan pemurnian, dilakukan penambahan eksipien dan dijerap dengan ajuvan aluminium. Vecon Pediatric® tidak mengandung bahan pengawet.

Seperti apa bentuk Vecon Pediatric®?
Vecon Pediatric® ini berupa suspensi berwarna putih susu dengan endapan bertingkat yang dapat didispersikan dengan cara dikocok. Vecon Pediatric® tersedia dalam dosis tunggal *prefilled syringe.*

Apa yang terkandung dalam Vecon Pediatric®?
Dalam setiap 0,5mL Vecon Pediatric® terdapat 10µg *Hepatitis B Surface Antigen* dengan zat tambahan Natrium klorida 4,5mg, Aluminium kalium sulfat dodekahidrat 1,52mg dan Natrium hidroksida 0,385mg.

Untuk apa Vecon Pediatric® digunakan?
Digunakan sebagai imunisasi aktif untuk mencegah terjadinya infeksi yang disebabkan oleh virus Hepatitis B pada bayi baru lahir dan bayi di bawah 1 tahun, terutama pada bayi baru lahir dengan Ibu yang positif *Hepatitis B Surface Antigen* (HbsAg) dan/atau HBeAg.

Bagaimana cara pemberian Vecon Pediatric®?
Bayi baru lahir dan bayi di bawah 1 tahun yang rentan terhadap virus hepatitis B, terutama bayi baru lahir dengan Ibu yang positif *Hepatitis B Surface Antigen* (HbsAg) dan/ atau HbeAg, akan menerima tiga suntikan (0,5mL tiap dosis) vaksin primer pada jadwal 0, 1 dan 6 bulan. Suntikan pertama pada bayi baru lahir harus diberikan dalam waktu 24 jam setelah lahir. Vecon Pediatric® diberikan melalui secara intramuskular. Pada bayi baru lahir dan bayi di bawah 1 tahun, Vecon Pediatric® diberikan melalui otot paha.

Tenaga kesehatan Anda akan menentukan apakah anak Anda dapat diberikan Vecon Pediatric® atau tidak.

Siapa yang tidak boleh divaksinasi dengan Vecon Pediatric®?

- Individu yang memiliki riwayat alergi terhadap komponen vaksin, termasuk eksipien dan formaldehida.
- Individu yang memiliki riwayat penyakit akut, penyakit kronis berat, penyakit kronis eksaserbasi akut, atau demam.
- Individu dengan riwayat alergi terhadap vaksin kombinasi Hepatitis A & B atau vaksin Hepatitis B.
- Individu yang memiliki riwayat epilepsi tidak terkontrol atau penyakit progresif lainnya pada sistem saraf.

Laporkan ke dokter atau tenaga kesehatan jika anak Anda memiliki salah satu dari kondisi di atas.

Apa yang perlu diperhatikan saat menggunakan Vecon Pediatric®?

Bicarakan dengan dokter atau tenaga Kesehatan sebelum vaksinasi jika anak Anda:

- Memiliki riwayat atau keluarga dengan riwayat kejang, dan/atau memiliki penyakit kronis, riwayat epilepsi, atau kecenderungan alergi.
- Mengalami reaksi abnormal seperti demam tinggi atau kejang setelah vaksinasi pertama.
- Bayi baru lahir dengan Ibu yang posititif HBsAg dan/atau HBeAg harus mengikuti petunjuk dokter apakah dapat menerima suntikan kedua dan ketiga.
- Bayi lahir sangat prematur (usia kehamilan ≤30 minggu), karena beberapa kondisi abnormal mungkin terjadi setelah vaksinasi.

Obat dan makanan apa yang harus dihindari jika mendapatkan Vecon Pediatric®?

Belum terdapat informasi terkait obat atau makanan yang harus dihindari ketika mendapatkan Vecon Pediatric®.

Pemberian bersamaan dengan obat imunosupresif, termasuk imunosupresan, obat kemoterapi, agen alkilasi, obat sitotoksik, dan kortikosteroid dapat mengurangi respons imun tubuh terhadap vaksin Hepatitis B. Laporkan ke dokter atau tenaga kesehatan jika Anda sedang menjalani pengobatan sebelum mendapatkan Vecon Pediatric®.

Dapatkah saya mengemudi atau mengoperasikan mesin setelah mendapatkan Vecon Pediatric®?

Vecon Pediatric® tidak berpengaruh terhadap kemampuan mengemudi dan mengoperasikan mesin. Namun, beberapa efek samping dapat memengaruhi kemampuan mengemudi atau menggunakan mesin untuk sementara.

Apa efek samping yang mungkin terjadi setelah pemberian Vecon Pediatric®?

Berdasarkan laporan uji klinis, efek samping yang mungkin terjadi dapat berupa reaksi lokal dan reaksi sistemik. Reaksi lokal yang umum dilaporkan berupa nyeri, demam, indurasi dan mukosa kulit, reaksi alergi, mual dan muntah, bengkak, ertiema, kelelahan dan astenia, menangis, dan gangguan laktasi atau makan. Gejala-gejala ini dilaporkan bersifat ringan hingga sedang. Umumnya, tidak diperlukan pengobatan khusus dan gejala dapat hilang dalam beberapa hari setelah vaksinasi. Jika diperlukan, pengobatan simtomatik dapat diberikan.

Eferk samping yang jarang terjadi dapat berupa Thrombocytopenic purpura, thrombocytopenia dan Anoreksia.

Jika terjadi efek samping lain selain yang tertera diatas, segera hubungi dokter atau tenaga kesehatan.

Masyarakat dapat melaporkan efek samping ke Bio Farma melalui call center Bio Care : 1500810.

Seperti apa tanda/gejala kelebihan dosis dalam pemberian Vecon®?

Kelebihan dosis pada pemberian produk ini tidak mungkin terjadi karena produk berupa jarum suntik yang sudah berisi 1 dosis vaksin.

Bagaimana cara penyimpanan Vecon Pediatric®?
Vecon Pediatric® disimpan pada suhu 2-8°C dan terlindung dari cahaya. Vaksin ini tidak boleh dibekukan. Selama penyimpanan, endapan putih dan cairan bening dapat terlihat. Ini bukan merupakan tanda kerusakan. Dokter atau tenaga kesehatan akan mengocok dengan baik untuk memperoleh suspensi putih yang homogen sebelum mengeluarkan udara dari jarum suntik, dan memeriksa secara visual untuk setiap partikel dan/atau perubahan aspek fisik sebelum pemberian. Dokter atau tenaga kesehatan tidak akan menggunakan vaksin jika ada benda asing di dalam isinya, atau sudah melewati tanggal kadaluwarsa yang tertera pada dus dan label.

Berapa lama Vecon Pediatric® dapat digunakan setelah kemasan dibuka?
Vecon Pediatric® harus segera diberikan setelah kemasan dibuka.

Kemasan:
Suspensi injeksi
Vecon Pediatric®: Dus, 1 Pre-Filled Syringe (PFS) @10 µg/0,5 mL (1 dosis)

No. Reg:

Diproduksi oleh: Shenzhen Kangtai Biological Products Co., Ltd
No.18, Shutianpu Road, Matian Street, Guangming District, Shenzhen, China

Diimpor oleh: PT Bio Farma (Persero)
Jl. Pasteur No. 28 – Bandung 40161 - Indonesia

Harus Dengan Resep Dokter