Size : 175 x 150 mm

PRESCRIBING INFORMATION

EasySix™

Fully Liquid Hexavalent Vaccine

NAME OF THE MEDICINAL PRODUCT

Trade/ Brand Name: EasySix™ Vaccine (DTwP-Hib-Hep B-IPV)
Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA), Poliomyelitis (Inactivated) and *Haemophilus influenzae* Type b Conjugate Vaccine (Adsorbed) IP

QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose of 0.5 ml contains:

Diphtheria Toxoid	⩾30 IU
Tetanus Toxoid	⩾60 IU
Inactivated Whole cell Pertussis	⩾4 IU
r Hepatitis B surface antigen	⩾10 µg
Haemophilus influenzae type b conjugated to 18-33 µg Tetanus toxoid (carrier protein)	10 µg
Inactivated Salk Polio Virus type 1*	40 DU
Inactivated Salk Polio Virus type 2*	8 DU
Inactivated Salk Polio Virus type 3*	32 DU
Aluminium content (Al3+) (As Aluminium Phosphate Gel)	NMT 1.25 mg
2-phenoxyethanol	3.3 mg
Physiological saline	q.s.

* Bulk source: Bilthoven Biologicals B.V., Netherlands;
Cell substrate: Vero cells

DOSAGE FORM AND STRENGTH

Liquid suspension for injection.
Single-dose vial containing 0.5 ml vaccine
Multi-dose vial containing 2.0 ml / 4 dose vaccine
Single-dose Pre-filled syringe containing 0.5 ml vaccine .

CLINICAL PARTICULARS

Therapeutic indication

For active immunization of infants against Diphtheria, Tetanus, Pertussis (Whooping Cough), Hepatitis B, infections caused by *Haemophilus influenzae* (Type b) & Poliomyelitis.

Posology

Primary immunization

EasySix™ is indicated for active immunization of infants, it is recommended that the primary vaccination schedule consists of three doses of 0.5ml each administered with an interval of four weeks between doses, starting at 6 weeks of age. The customary age for the first dose of primary immunization is recommended to be 6 weeks of age.
Specifically, WHO recommends 6, 10, and 14 weeks primary series schedule for Diphtheria, Tetanus, Whole-cell pertussis (DTwP), Hepatitis B (Hep B), *Haemophilus influenza* type b conjugate (Hib) and Inactivated Poliomyelitis trivalent (IPV)
The interval can vary from 4-to 8 weeks.
A booster dose of DTwP is recommended at the age of 12-23 months.

Booster immunization

The booster dose of Hep B, Hib, and IPV can be given ⩾6 months after the last primary dose.
Accordingly booster dose of EasySix™ Vaccine can be administered at 12-15 months.

Method of Administration

For intramuscular use only.
Just before use, shake the vial or syringe until a uniform, white, cloudy suspension results. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, the product should not be administered. Administer a single 0.5 mL dose of EasySix™ Vaccine intramuscularly.
In infants younger than 1 year, the anterolateral aspect of the thigh is the preferred site of injection. The vaccine should not be injected into the gluteal area. EasySix™ Vaccine should not be combined through reconstitution or mixed with any other vaccine. Discard unused portions.
The vaccination should be given by medical or healthcare professionals who are trained in the use of vaccines and who are equipped to deal with any uncommon severe allergic reaction to the injection.
Do not inject intravenously or subcutaneously.

Contraindications

EasySix™ should not be administered to subjects with known Hypersensitivity to any component of the vaccine or to subjects who have shown signs of hypersensitivity after the previous administration of Diphtheria, Tetanus, Pertussis, Hepatitis B, Hib, and IPV vaccines.

Other medicines or vaccines and EasySix™

Tell your doctor or pharmacist if your child is taking, has recently taken any other medicines or might take any other medicines.
EasySix™ can be given at the same time as other vaccines such as pneumococcal polysaccharide conjugate vaccines, measles-mumps-rubella vaccines or rotavirus vaccines.
Your doctor will give the injections at different sites and will use separate syringes and needles for each injection.

Special warnings and precautions for use

EasySix™ vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and the possible occurrence of undesirable events) and a clinical examination.
If any of the following events occur in temporal relation to the administration of EasySix™ vaccine the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered:

- Temperature of ⩾40.0˚C within 48 hours, not due to another identifiable cause
- Collapse or shock-like state (hypotonic-hypo responsive episode) within 48 hours
- Persistent crying lasting >3 hours, occurring within 48 hours
- Convulsions with or without fever, occurring within 3 days.

A history of febrile convulsions, a family history of convulsions, a family history of SIDS (Sudden Infant Death Syndrome) or a family history of an adverse event following EasySix™ vaccination does not constitute contra-indications.
HIV infection is not considered as a contra-indication for diphtheria, tetanus, pertussis, hepatitis B, Hiib and polio vaccination. The expected immunological response may not be obtained after vaccination of Immunosuppressed patients, e.g. 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 vaccine should remain under medical supervision for 30 minutes after vaccination.

Drugs Interactions

Co-administration with other vaccines

EasySix™ Vaccine may be administered simultaneously with pneumococcal polysaccharide conjugate vaccines, rotavirus vaccines, measles, mumps, rubella (MMR), and varicella containing vaccines and meningococcal C conjugate vaccines. The safety and immunogenicity of EasySix™ Vaccine do not change significantly when co-administered with other vaccines included in the child's vaccination schedule.
Co-administration of EasySix™ Vaccine with other injectable vaccines must be carried out at separate injection sites and, preferably, separate limbs.
EasySix™ Vaccine should not be mixed with any other vaccine or other parenterally administered medicinal products.

Use in special populations (such as pregnant women, lactating women, pediatric patients, geriatric patients, etc.)

Pregnancy and Lactation

As EasySix™ Vaccine is not intended for use in adults, information on the safety of the vaccine when used during pregnancy or lactation is not available.

Pediatric Use

Premature infants

EasySix™ Vaccine can be given to preterm infants, however, as expected in this population, a lower immune response can be observed for some antigens and the level of clinical protection is unknown. Also, the potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very preterm infants (born ⩽ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in these infants, vaccination should not be withheld or delayed.

Effects on ability to drive and use machines

Although no such studies have been performed, it is expected that EasySix™ Vaccine would have no or negligible influence on the ability to use bicycles and other such machines.

Undesirable Effects

Like all medicines, EasySix™ can cause side effects, although not everybody gets them.
In a randomized clinical study of EasySix™ in healthy infants following adverse events were reported.
Very common: ≥ 1/10, Common: ≥ 1/100 to <1/10, Uncommon: ≥1/1000 to <1/100, Rare: ≥1/10000 to <1/1000, Very rare: <1/10000.

System Organ Class	Frequency	Adverse events
General disorders and administration site conditions	Very common	Pain/ tenderness, Fever, Swelling, Redness
Psychiatric disorders	Common	Irritability /restlessness/ fussiness
Gastrointestinal disorders	Common	Vomiting
Nervous system disorders	Uncommon	Excessive sleepiness/ drowsiness
Gastrointestinal disorders	Rare	Diarrhoea
Metabolism and nutrition	Rare	Poor eating

Most of these symptoms were resolved within 48 hours after vaccination.

Other side effects:

Serious allergic reactions are a very rare possibility, If any of these symptoms occur after leaving the place where your child received his/her injection, you must consult a doctor IMMEDIATELY:

- difficulty in breathing
- a rash
- swelling of the face or throat
- low blood pressure causing dizziness or collapse.

When these signs or symptoms occur they usually develop quickly after the injection is given and while the child is still in the clinic.
Other side effects not listed above have been reported occasionally with other diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B or Hib containing vaccines and not directly with EasySix™ are temporary inflammation of nerves causing pain, paralysis, and sensitivity disorders (Guillain-Barre syndrome/ GBS) and severe pain and brachial neuritis have been reported after administration of a tetanus-containing vaccine, inflammation of nerves or polyradiculoneuritis, facial paralysis, loss of vision, uveitis, central nervous system demyelination, multiple sclerosis have been reported after administration of a hepatitis B antigen containing vaccine.
If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are

Size : 175 x 150 mm

asked to report any suspected adverse reactions to pvg@panaceabiotec.com OR Mobile No. +91-9650138282

Overdose

Experience of overdose is limited.

There is no specific treatment for an overdose with EasySix™ Vaccine. In the event of an overdose, the infant should be monitored and provided with symptomatic treatment as appropriate.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action

Diphtheria

Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of C. diphtheriae. Protection against disease is due to the development of neutralizing antibodies to diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of ⩾0.1 IU/mL are generally regarded as protective. (6) Levels of 1.0IU/mL have been associated with long-term protection.

Tetanus

Tetanus is an acute disease caused by an extremely potent neurotoxin produced by C. tetani. Protection against disease is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of ⩾ 0.01 IU/mL, measured by neutralization assay is considered the minimum protective level. (6) (8) A tetanus antitoxoid level ⩾ 0.1 IU/mL as measured by the ELISA used in clinical studies of VAXELIS is considered protective.

Pertussis

Pertussis (whooping cough) is a respiratory disease caused by B. pertussis. This Gram-negative coccobacillus produces a variety of biologically active components, though their role in either the pathogenesis of, or immunity to, pertussis has not been clearly defined.

Poliomyelitis

Polioviruses, of which there are 3 serotypes (Types 1, 2, and 3), are enteroviruses. The presence of poliovirus type-specific neutralizing antibodies has been correlated with protection against poliomyelitis.

Hepatitis B

Hepatitis B virus is one of several hepatitis viruses that cause systemic infection, with major pathology in the liver. Antibody concentrations of ⩾ 10 mIU/mL against HBsAg correlate with protection against hepatitis B virus infection.

***Haemophilus influenzae* type b**

H. influenzae type b can cause invasive diseases such as meningitis and sepsis. The anti-PRP antibody has been shown to correlate with protection against invasive disease due to H. influenzae type b. Based on data from passive antibody studies (10) and an efficacy study with H. influenzae type b polysaccharide vaccine in Finland, (11) a post-vaccination anti-PRP level of ⩾ 0.15 mcg/mL is considered a minimal protective level. Data from an efficacy study with H. influenzae type b polysaccharide vaccine in Finland indicate that an anti-PRP level of ⩾ 1.0 mcg/mL 3 weeks after vaccination predicts protection through a subsequent 1-year period. (11) (12) These levels have been used to evaluate the effectiveness of H. influenzae type b conjugate vaccines.

Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined.

Immunogenicity

Immunogenicity of EasySix™ vaccine was evaluated in 6, 10, 14 weeks schedule (3-doses given at 4 weekly intervals). The seroprotection rates/ immune responses for all components of the vaccine after 1-month completion of the 3-dose primary vaccination schedule were as follows: Anti-diphtheria, anti-tetanus, and anti-HBsAg seroprotection rate was 94.85%, 100%, and 97.79%, respectively. The anti-PRP seroprotection rate was 100% for the short term and 92.65% for long-term protection. The pertussis IgG and anti-PT response rate was 75.74% and 68.38%, respectively. The Seroconversion rate against polio type 1, type 2, and type 3 was 89.71%, 93.38%, and 88.24%, respectively.

Differences in Seroprotection/Immune Response Rates between Groups, with 95% CIs (Immunogenicity Cohorts)

Antigen	EasySix™ (N = 136)	Threshold (N = 136)	Pentavac SD® co administered with Imovax Polio® Polio® - EasySix™)	Difference in Seroprotection Rate (Pentavac SD® co-administered with Imovax		
					95 % CI	
	n (%)		n (%)	Difference in %	LL	UL
Anti-Diphtheria	129(94.85)	⩾ 0.1 IU/ml	130(95.59)	0.74	-4.334	5.805
Anti-Tetanus	136(100)	⩾ 0.1 IU/ml	136(100)	0	NA	NA
Anti-PRP (Short term)	136(100)	⩾ 0.15 µg/ml	136(100)	0	NA	NA
Anti-PRP (Long term)	126(92.65)	⩾ 1 µg/ml	121(88.97)	-3.68	-10.529	3.176
Anti-HBs	133(97.79)	⩾ 10mIU/ml	132(97.06)	-0.73	-4.497	3.027
Anti-PT	93(68.38)	⩾100 µg/ml and 4 fold	90(66.18)	-2.20	-13.355	8.942
Pertussis IgG	103(75.74)	⩾18 IU/ml and 4 fold	99(72.79)	-2.95	-13.326	7.443
Anti-Polio Type 1	122(89.71)	⩾8 (1/dilution)	125(91.91)	2.20	-4.655	9.067
Anti-Polio Type 2	127(93.38)	⩾8 (1/dilution)	128(94.12)	0.74	-5.017	6.488
Anti-Polio Type 3	120(88.24)	⩾8 (1/dilution)	123(90.44)	2.20	-5.124	9.536

Pharmacokinetic properties

Not applicable

NONCLINICAL PROPERTIES

Animal Toxicology or Pharmacology

Panacea Biotec conducted an exclusive toxicity study of EasySix™ (DTwP -HepB - Hib - IPV) vaccine to assess the safety of the vaccine in combination form in animal model i.e., New Zealand White Rabbits by intramuscular route, the intended clinical route.

- **Single-Dose Toxicity and Local Tolerance Study of EasySix™ Vaccine in New Zealand White Rabbits by Intramuscular Route**

Based on the results, it is concluded that the EasySix™ vaccine was well tolerated up to the dose level of 1.0 mL/rabbit when administered by intramuscular injection in divided doses of 0.5 mL/site in the quadriceps muscles of the hind limbs and did not produce any toxicity under the conditions and

- **Repeated Dose Toxicity Study of EasySix™ Vaccine in New Zealand White Rabbits by Intramuscular Route (N+1 =4 Schedule).**

Based on the above findings, it is concluded that the EasySix™ vaccine did not produce any adverse effect up to 1.0 mL /rabbit (0.5 mL/ site) in New Zealand White rabbits when administered repeatedly following the N+1=4 schedule.

DESCRIPTION

EasySix™ vaccine is light pink to off-white suspension in which the mineral carrier (aluminium phosphate gel) tends to settle down slowly on keeping. Easy Six Vaccine is a vaccine to protect infants and toddlers against infectious diseases such as Diphtheria, Tetanus, Pertussis, Poliomyelitis, Hepatitis B & severe infections caused by *Haemophilus influenzae* Type b.

Easy Six Vaccine is administered by injection to infants and toddlers starting from the age of 6 weeks. It is usually given at 6, 10, and 14 weeks followed by a booster dose in the second year of life. If the child does not get all the doses, he/she will not be fully protected against the virus and bacteria.

PHARMACEUTICAL PARTICULARS

Incompatibilities

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

Shelf-life

The expiry date of the vaccine is indicated on the label and packaging.

Multi- Dose vials of EasySix from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions, for up to a maximum of 28 days considering:

- The expiry date of the vaccine has not passed
- The vaccine vial has been and continues to be stored at the recommended temperatures; furthermore, the vaccine vial monitor, if one is attached, is visible on the vaccine label and is not past its discard point and the vaccine has not been damaged by freezing.

Packaging information

Single dose vial containing 0.5 ml vaccine

Multi dose vial containing 2.0 ml / 4 dose vaccine

Single dose Pre-filled syringe containing 0.5 ml vaccine supplied along with 25G needle of 1".

Storage and handling instructions

EasySix™ Vaccine should be stored at 2°C to 8°C (36°F to 46°F). Do not freeze. The vaccine which has been exposed to freezing should not be used. Protect from light. Do not use after the expiration date shown on the label. Discard unused portions.

PATIENT COUNSELLING INFORMATION

Advise the patient to read the approved patient labeling (Patient Information).

Inform the parent or guardian of the following:

The potential benefits and risks of immunization with EasySix™ Vaccine.

The common adverse reactions that have occurred following the administration of EasySix™ Vaccine.

Other adverse reactions can occur. Call your doctor with any adverse reactions of concerns.

DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Market Authorization No.: MB/07/632

Date of Authorization: 02 January 2017

Manufactured by:
Panacea Biotec Ltd.
Malpur, Baddi,
Distt. Solan (H.P.) - 173205, India.

Panacea Biotec
Innovation in support of life

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