TETRAct-HIB
HAEMOPHILUS TYPE b CONJUGATE VACCINE
AND COMBINATION ADSORBED DIPHTERIA,
TETANUS AND PERTUSSIS VACCINE

COMPOSITION
HAEMOPHILUS TYPE b CONJUGATE VACCINE (lyophilisate for one immunizing dose).
- *Haemophilus influenzae* type b polysaccharide conjugate to tetanus protein\(^{(1)}\) ... 10 μg
- Trometamol .................................................................0,6 mg
- Sucrose ...........................................................................42,5mg

DIPHTHERIA-TETANUS-PERTUSSIS VACCINE (suspension for injection for one vaccinating dose):
- Purified diphtheria toxoid\(^{(2)}\) ..............................................................not less than 30 IU
- Purified tetanus toxoid \(^{(3)}\) .................................................................not less than 60 IU
- *Bordetella pertussis*\(^{(4)}\) ..............................................................not less than 4 IU
- Alumunium hydroxide (expressed as Al) .............................................not more than 1,25mg
- Thiomersal ..............................................................................not more than 0,05mg
- 0,9% sodium chloride solution.......................................................up to 0,50 ml

\(^{(1)}\) Strain 1472 IM 2164
\(^{(2)}\) Strain 1514-N-3S
\(^{(3)}\) Strain 1472 C
\(^{(4)}\) Strain 1414, 1416

PHARMACEUTICAL FORM
Suspension for injection obtained by reconstitution of the lyophilisate in one vial of *Haemophilus influenzae* type b with one syringe of D.T.P. for administration by intramuscular or subcutaneous route.

MARKETING AUTHORIZATION HOLDER AND MANUFACTURER
SANOFI PASTEUR SA-2, avenue Pont Pasteur 69007 Lyon-France

THERAPEUTIC INDICATIONS
This dru is a VACCINE.
This drug is recommended, from 2 months of age, for the combined prevention of invasive infections such as meningitis, septicemia, epiglotitis caused by *Haemophilus influenzae* type b and of diphtheria, tetanus and pertussis.

TETRAct-HIB does not protect against other diseases caused by other types of *Haemophilus influenzae*, nor against meningitis of other origins.

The *Haemophilus influenzae* type b component of TETRAct_HIB is indicated for children until the age of 5 years.

**CONTRA-INDICATIONS**

This medicine MUST NOT BE USED in the following cases:

– Hypersensitivity to any component of the vaccine
– Evolving encephalophaty with or without convulsions.
– The vaccine is contra-indicated in subjects having shown one or more of the following responses during the first 48 hours after vaccination.
  • Fever greater than or equal to 40°C.
  • High pitched crying
  • Convulsions (due to the benign aspect of these febrile seizures, these would not in theory be a source of contra-indications).
  • Allergic reactions

**PHARMACOLOGICAL PROPERTIES**

*Haemophilus type b Conjugate Vaccine*

Protects against invasive disease caused by *Haemophilus influenzae* type b.

The capsular polysaccharide (polyribosyl ribitol phosphate: PRP) induces a serological anti PRP response when administered to humans.

However, as with all the polysaccharide antigens, the antibody response is thymo-independent, characterized by the absence of a booster effect after repeated injections and by weak immunogenicity in infants.

The covalent binding to a protein, the tetanus protein of the capsular polysaccharide of *Haemophilus influenzae* type b, gives a T-cell dependent immunogenic property inducing in infants an Ig G specific anti PRP response with an immunological memory.

Study of the functional activity of the specific anti PRP antibodies, induced by the Haemophilus type b conjugate vaccine in infants and children, showed bactericidal as well as opsonizing properties.
The immunogenicity studies in infants vaccinated from the age of 2 months have shown that, on average 90% of them had an anti-PRP titer > 0,15μg/ml after the 2nd dose of Haemophilus type b conjugate vaccine, and nearly all of them after the 3rd dose. The anti-PRP titer exceeds 1 μg/ml in about 90% of them after the 3rd dose. In infants of 3 to 4 months having received three doses of μg/ml conjugate vaccine, a booster injection carried out 8 to 12 months later, either with Haemophilus type b conjugate vaccine or a non-conjugated polysachharide vaccine, resulted in a very significant increase (of a factor greater than 10) of the average anti-PRP antibody titer.

This demonstrates the induction of immunological memory created by the initial injection of Haemophilus type b conjugate vaccine and suggests that in the case of a natural infection in the vaccinated infant, the bacteria capsule should induce a comparable anamnestic effect. Studies in children of 12 to 24 months have shown a seroconversion (anti-PRP > 1 μg/ml) in more than 80% after a single dose of Haemophilus type b conjugate vaccine.

Diphtheria – Tetanus – Pertussis Vaccine
This vaccine is prepared by blending of diphtheria and tetanus toxins, detoxified by formaldehyde and purified pertussis bacilli inactivated by heat. Immunity appears shortly after the second injection. It is reinforced after the third injection and lasts for at least 5 years after the first booster.

PRECAUTION FOR USE
KEEP OUT OF REACH OF CHILDREN

DRUG INTERACTIONS
− Children receiving immunosupresive therapy may have a reduce response to active immunization procedures.
− As with other intramuscular injection TETRAct-HIB should be given with caution to children on anticoagulant therapy.
− Tetanus immune globulin or diphtheria antitoxin, if used should be given in separate site with a separate needle and syringe.
− Influenzae virus vaccine should not be administered within 3 days of immunization with a pertussis containing vaccine since both vaccine may cause febrile reactions in young children.

WARNINGS
As with any other vaccination, an injection should be delayed in the presence of fever or acute infections.
As with any intramuscular injection, TETRAct-HIB should be given with caution infants or children with thrombocytopenia or any coagulation disorder that would contraindicate in intramuscular injection. Previous history of convulsions not related to previous vaccination is not a contraindication for vaccination. Nevertheless, it can be useful to associate with vaccination, as a preventive, antiepileptics and/or antipyretics.

POSOLOGY AND METHOD OF ADMINISTRATION

TO BE ALWAYS TAKEN ONLY IN ACCORDANCE WITH THE PRESCRIPTION OF YOUR DOCTOR

As a guide:
3 injections of a unitary dose of the vaccine (0.5 ml) at one or two months interval.
The official schedule recommends an injection at 2, 3 and 4 months of age, followed by a booster injection administered one year after the primo-vaccination.
The vaccine is administered in the antero-lateral region of the thigh (middle third) by intramuscular or subcutaneous route.
However, because the D.T.P. vaccine is adsorbed, the intramuscular route should be preferred, in order to minimize the potential adverse reactions.
When giving the injection, make sure that the needle does not penetrate a blood vessel. Do not inject by intravascular route.

INSTRUCTION FOR USE

Reconstitute the HAEMOPHILUS TYPE b CONJUGATE VACCINE (lyophilisate) with the D.T.P. suspension.
Shake until complete dissolution of the lyophilisate: the cloudy, whitish appearance of the suspension after reconstitution is normal.

SIDE EFFECTS

From D.T.P. they are:
- Local reactions at the injection site: pain, redness, induration, oedema, sometimes subcutaneous nodules.
  Incidence and severity of local reactions may potentially be influenced, depending on subjects, by site, route, method of administration and number of prior dose.
- Systemic reaction:
– Fever greater than 39°C, insomnia, irritability or unusual crying, transient (24 to 48 hours) can be observed in 40% of vaccinated children. They are associated with one or more convulsions in rare cases;
– Hypotonic hyporesponsive episode : exceptional with spontaneous healing;
– High pitched crying;
– Allergic reactions to different components of the product;
– Acute encephalopathy with an estimated rare between 0.1 and 1 for 100,000 injections complicated by neurologic sequelae with an estimated rate between 0.02 and 2 for 100,000 injections.

From Haemophilus type b conjugate vaccine they are:
More than 110,000 doses of Haemophilus type b conjugate vaccine were administered to infants and children and no serious adverse reactions, local or systemic, related to the vaccine were reported.
In case of simultaneous injections of D.T.P. vaccine and Haemophilus type b conjugate vaccine infants from 2 to 6 months, the severity and frequency of the side effects have not been different from those recorded when D.T.P. vaccine was injected alone.

OTHER POSSIBLE EFFECT
Like any active product, this drug may, in some people, cause mild or more serious side effects:
– Convulsions,
– Acute reaction induced by a former injection of pertussis vaccine.

SHELF LIFE
DO NOT USE AFTER THE EXPIRY DATE CLEARLY INDICATED ON THE PACKAGING.

SPECIAL PRECAUTIONS FOR STORAGE
This vaccine should be kept refrigerated between +2°C and +8°C.
Do not freeze.

Imported by:
PT. Aventis Pharma, Jakarta, Indonesia
For PT. BIO FARMA, Bandung
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