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The vaccines division of sanofi-aventis Group

Summary of Product Characteristics

Product Name	095UN_ACT-HIB
INN	*Haemophilus Influenzae* type b vaccine (conjugated)
Date of last French license (current)	16 avril 2009
Document ID:	[eDoc C6 TBD]
Language	English
Document Tracking	Updated sections : • 4.4 : addition of paragraph "Apnoea in very premature infants" • 4.8 : addition of paragraph "Apnoea in very premature infants" ***Anne Dubost-Eyraud***

1 NAME OF THE MEDICINAL PRODUCT

ACT-HIB 10 micrograms/0.5 ml, powder and solvent for solution for injection in a pre-filled syringe

***Haemophilus Influenzae* type b vaccine (conjugated)**

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Haemophilus influenzae type b polysaccharide	10 micrograms
conjugated to tetanus protein.....	18-30 micrograms

for one 0.5 ml dose of reconstituted solution.

For a list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection in a pre-filled syringe.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

This vaccine is indicated for the prevention of *Haemophilus influenzae type b* invasive infections (meningitis, septicaemia, cellulitis, arthritis, epiglottitis, etc.) in children from the age of 2 months.

This vaccine does not provide protection against infections due to other types of *Haemophilus influenzae* or against cases of meningitis of other origins.

Under no circumstances can the tetanus protein contained in this vaccine be used to replace the usual tetanus vaccination.

4.2 Posology and Method of Administration

Posology

- Before 6 months of age, 3 successive doses of 0.5 ml administered one or two months apart, followed by a booster injection (fourth dose) one year after the third injection.

- Between 6 and 12 months of age, 2 doses of 0.5 ml administered one month apart, followed by a booster injection (0.5 ml) at 18 months of age.
- From 1 to 5 years of age, a single dose of 0.5 ml.

For contact cases: in the event of contact with a case of invasive *Haemophilus influenzae* type b disease (family or childcare), vaccination should be implemented according to the schedule for the contact case's age.

The index case should also be vaccinated.

Method of Administration

Intramuscular or deep subcutaneous route.

The recommended injection sites are the antero-lateral aspect of the thigh (middle third) for infants and toddlers and the deltoid region for older children.

Do not inject by the intravascular route.

For reconstitution instructions, see section 6.6.

4.3 Contraindications

Known hypersensitivity to one of the components of the vaccine, in particular the tetanus protein, or experienced after a previous injection of a *Haemophilus influenzae* type b conjugate vaccine.

4.4 Special Warnings and Precautions for Use

Warnings

Do not inject by the intravascular route: make sure that the needle does not penetrate a blood vessel.

In case of fever or acute illness, vaccination should be postponed.

As with any injectable vaccine liable to induce a potential immediate anaphylactic reaction, an appropriate medical treatment should be available.

Children with congenital or acquired immunodeficiency may be vaccinated, keeping in mind that, depending on the state of their immune system, their immune response will be lesser or greater. In children under immunosuppressive treatment (corticotherapy, antimitotic chemotherapy, etc.), it is recommended to postpone vaccination until the end of the treatment.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 h should be considered when administering the primary immunisation series to very premature infants (born $\leq$ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed

4.5 Interactions with Other Medicinal Products and Other Forms of Interaction

This vaccine may be administered simultaneously with another, such as the other recommended vaccines (against diphtheria, tetanus, pertussis, poliomyelitis, measles, mumps and rubella), provided that 2 injection sites are used.

4.6 Pregnancy and Lactation

Not applicable.

4.7 Effects on Ability to Drive and Use Machines

Not applicable.

4.8 Undesirable Effects

In accordance with childhood immunization schedules and the WHO (World Health Organisation) and ACIP (Advisory Committee on Immunization Practices) recommendations, Act-HIB is rarely administered alone, but often given in association or combination with other concomitant vaccines, such as vaccines containing diphtheria, tetanus, and pertussis antigens (whole-cell or acellular).

Therefore, the safety profile of Act-HIB will reflect this concomitant use.

Undesirable effects reported during clinical trials or post marketing are listed here using MedDRA terminology (by System Organ Class and frequency) for all age groups. The frequency classifications are as follows: very common (≥ 10 %), common: (≥ 1 % and < 10 %), uncommon (≥ 0.1 % and < 1 %), rare (≥ 0.01 % and < 0.1 %), very rare (< 0.01 %), including isolated reports.

Undesirable Effects Observed During Clinical Trials:

The safety of the vaccine was evaluated in the course of different controlled clinical studies including active surveillance of undesirable effects, and during which more than 7,000 healthy children younger than 2 received an Act-HIB injection, almost always in combination with a whole cell or acellular diphtheria-tetanus-pertussis vaccine.

In controlled studies, when Act-HIB was administered in combination with DTP vaccines, the frequency and type of subsequent systemic reactions observed were not different from those seen with a DTP vaccine administered alone.

Undesirable effects, possibly related to the vaccine and observed with a frequency of more than 1%, generally appeared in the 6 to 24 hours after vaccination and were, for the most part, transient and of mild to moderate intensity.

No increase in the incidence or severity of these local or systemic reactions was seen with successive doses of the primary vaccination series.

General disorders and anomalies at the injection site

Very common to common: injection-site reactions such as pain, erythema, swelling and/or inflammation, induration

Uncommon: fever (>39 °C).

Psychiatric disorders
Very common: irritability.
Common to uncommon: crying (uncontrollable or abnormal).

Undesirable Effects Observed Post Marketing

In the course of post-marketing surveillance following extensive administration (several million doses worldwide), other reactions have been reported in temporal association with the vaccine.

None of the following undesirable effects was reported with a frequency of more than 0.01 % (very rare). The frequencies are based on the rate of spontaneous notification and calculated from the number of notifications and the number of doses distributed during the same period.

General disorders and anomalies at the injection site
Very rare: oedema of the lower limbs with cyanosis or transient purpura appearing in the first few hours following vaccination and resolving quickly and spontaneously without sequelae. These reactions are not accompanied by cardio-respiratory symptoms. They were mainly reported when the vaccine was administered in combination with other vaccines (such as vaccines containing the diphtheria, tetanus and pertussis antigens).

Immune system disorders
Very rare: hypersensitivity reactions.

Nervous system disorders
Very rare: convulsions with or without fever.

Skin and subcutaneous tissue disorders
Very rare: urticaria, rash, pruritus.

Apnoea in very premature infants (born $\leq$ 28 weeks of gestation)(see section 4.4).

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

VACCINE AGAINST *HAEMOPHILUS INFLUENZAE* TYPE B INFECTIONS

(J: anti-infectious)

The *Haemophilus influenzae* type b vaccine provides immunity against *Haemophilus influenzae* type b invasive infections.

In humans, the capsular polysaccharide (polyribosil ribitol phosphate: PRP) induces an anti-PRP serological response. However, as for any polysaccharide antigen, the nature of the immune response is thymo-independent, characterised by the absence of a booster effect when repeated injections are performed and by a low immunogenicity in infants and toddlers. The covalent bond of the *Haemophilus influenzae* type b capsular polysaccharide to the tetanus protein enables the conjugate vaccine to behave like a thymo-dependent antigen, resulting in a specific anti-PRP serological response in infants and toddlers with the induction of specific IgG and the establishment of an immune memory.

The study of the functional activity of the PRP-specific antibodies induced by the *Haemophilus influenzae* type b conjugate vaccine in infants and toddlers, and children demonstrated their bactericidal and opsonising activities.

Immunogenicity studies in infants and toddlers vaccinated from 2 months of age demonstrated that practically all of them had an anti-PRP antibody titre ≥ 0.15 µg/ml after administration of the third dose (and ≥ 1 µg/ml for approximately 90 % of them). In infants younger than 6 months of age who received three doses of *Haemophilus influenzae* type b conjugate vaccine, a booster injection administered 8 to 12 months later induced a very significant increase in the mean titre of the PRP antibodies.

5.2 Pharmacokinetic Properties

Not applicable.

5.3 Preclinical Safety Data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Powder: trometamol, sucrose.

Solvent: sodium chloride, water for injections.

6.2 Incompatibilities

This vaccine should not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf Life

3 years.

6.4 Special Precautions for Storage

Store in a refrigerator (2°C—8°C)

Do not freeze.

6.5 Nature and Contents of Container

Powder in a vial (type I glass) + 0.5 ml of solvent in a pre-filled syringe (glass) with a plunger stopper (chlorobromobutyl)—box of 1.

Powder in a vial (type I glass) + 0.5 ml of solvent in a pre-filled syringe (glass) with a plunger stopper (chlorobromobutyl) and a tip cap (chlorobromobutyl) without needle—box of 1.

Powder in a vial (type I glass) + 0.5 ml of solvent in a pre-filled syringe (glass) with a plunger stopper (chlorobromobutyl) and a tip cap (chlorobromobutyl) with 2 separate needles—box of 1.

6.6 Instructions for Use, Handling and Disposal

Reconstitute the solution, either by injecting the content of the syringe of solvent into the vial of powder or by injecting the content of a syringe of combined diphtheria-tetanus-pertussis vaccine or diphtheria-tetanus-pertussis-poliomyelitis vaccine. Shake until the powder is completely dissolved. The whitish, cloudy appearance of the suspension following reconstitution by a syringe of diphtheria-tetanus-pertussis vaccine or diphtheria-tetanus-pertussis-poliomyelitis vaccine is normal.

For syringes without attached needle, the separate needle must be fitted firmly to the syringe, rotating it by a one-quarter turn.

7 MARKETING AUTHORIZATION HOLDER

SANOFI PASTEUR
2, AVENUE PONT PASTEUR
69007 LYON

8 PRESENTATIONS AND ADMINISTRATIVE IDENTIFICATION NUMBERS

- 334 720-1: Powder in a vial (type I glass) + 0.5 ml of solvent in a pre-filled syringe (type I glass) with a plunger stopper (chlorobromobutyl)—box of 1.
- 370 828-3: Powder in a vial (type I glass) + 0.5 ml of solvent in a pre-filled syringe (type I glass) with a plunger stopper (chlorobromobutyl) and a tip cap (chlorobromobutyl) without needle—box of 1.
- 370 830-8: Powder in a vial (type I glass) + 0.5 ml of solvent in a pre-filled syringe (type I glass) with a plunger stopper (chlorobromobutyl) and a tip cap (chlorobromobutyl) with 2 separate needles—box of 1.

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE MARKETING AUTHORIZATION

- Date of first authorization: 06 February 1992
- Date of renewal of the marketing authorization: 05 October 2006

10 DATE OF REVISION OF THE TEXT

16 avril 2009