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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ActHIB safely and effectively. See full prescribing information for ActHIB.

**ActHIB [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)]
Solution for Intramuscular Injection
Initial U.S. Approval: 1993**

INDICATIONS AND USAGE

- ActHIB is a vaccine indicated for the prevention of invasive disease caused by *Haemophilus influenzae* type b. ActHIB vaccine is approved for use as a four dose series in infants and children 2 months through 5 years of age (1)

DOSAGE AND ADMINISTRATION

For intramuscular administration only

Four-dose series (0.5 mL each) by intramuscular injection:

- A three-dose primary series administered at 2, 4, and 6 months of age. (2.1)
- A single booster dose administered at 15-18 months of age. (2.1)

DOSAGE FORMS AND STRENGTHS

Solution for injection: lyophilized powder to be reconstituted in supplied 0.4% Sodium Chloride diluent. A single dose, after reconstitution is 0.5 mL (3)

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any *H.*

influenzae type b or tetanus toxoid-containing vaccine or any component of ActHIB vaccine. (4)

WARNINGS AND PRECAUTIONS

If Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the potential benefits and risks of giving ActHIB vaccine must be evaluated. (5.2)

ADVERSE REACTIONS

Following administration of ActHIB vaccine in children 2-20 months of age, rates of adverse reactions varied by dose number and age of recipients:

- The most frequent systemic reactions after any dose for children 2 months to 16 months of age were fussiness/irritability (75%), inconsolable crying (58%) and decreased activity/lethargy (51%). (6.1)
- In children 15-20 months of age tenderness (20%) was the most common local reaction following a single dose. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pharmacovigilance Department, Sanofi Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 at 1-800-822-2463 (1-800-VACCINE) or VAERS at 1-800-822-7967 or <http://vaers.hhs.gov>.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: Month 201X

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1 **FULL PRESCRIBING INFORMATION:**

2

3 **1 INDICATIONS AND USAGE**

4 ActHIB® is a vaccine indicated for the prevention of invasive disease caused by *Haemophilus*
5 *influenzae* type b. ActHIB is approved for use in children 2 months through 5 years of age.

6

7 **2 DOSAGE AND ADMINISTRATION**

8 **For intramuscular use only**

9

10 **2.1 Immunization Series**

11 ActHIB vaccine is administered as a four-dose series (0.5 mL per dose) as:

- 12 • A primary three-dose series of a single dose at 2, 4, and 6 months of age.
13 • A single booster dose at 15 through 18 months of age.

14

15 **2.2 Reconstitution**

16 ActHIB vaccine is a solution for injection supplied as single-dose vials of lyophilized vaccine to
17 be reconstituted only with the accompanying saline diluent (0.4% Sodium Chloride). To
18 reconstitute ActHIB vaccine, withdraw 0.6 mL of saline diluent and inject into the vial of
19 lyophilized ActHIB vaccine. Agitate the vial to ensure complete reconstitution. The reconstituted
20 ActHIB vaccine will appear clear and colorless. Withdraw a 0.5-mL dose of the reconstituted
21 vaccine and inject intramuscularly. After reconstitution, if ActHIB vaccine is not administered

1 promptly store at 2° to 8°C (35° to 46°F) and administer within 24 hours. Stored vaccine should
2 be re-agitated prior to injection. Refer to Figures 1, 2, 3, and 4.

3 **Instructions for Reconstitution of ActHIB Vaccine with Saline Diluent (0.4% Sodium**
4 **Chloride)**

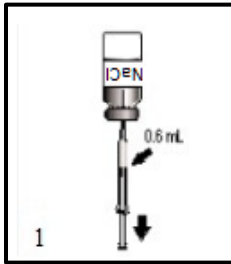


Figure 1.
Disinfect the diluent vial stopper, inject the needle and withdraw 0.6 mL of 0.4% Sodium Chloride diluent as indicated.

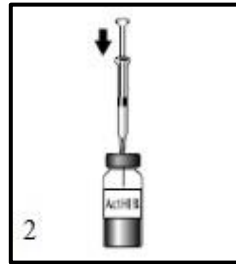


Figure 2.
Cleanse the ActHIB vaccine stopper, insert the syringe needle into the vial, and inject the total volume of diluent.



Figure 3.
Agitate vial thoroughly.

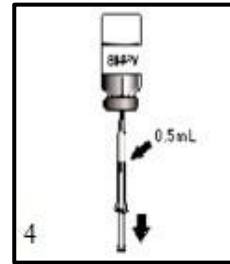


Figure 4.
After reconstitution, withdraw 0.5 mL of reconstituted vaccine and administer **intramuscularly**.

5

6

7 **2.3 Administration**

8 Parenteral drug products should be inspected visually for particulate matter and/or discoloration
9 prior to administration, whenever solution and container permit. If either of these conditions exist,
10 the vaccine should not be administered.

11

12 ActHIB vaccine is administered as a single dose (0.5 mL) by intramuscular injection into the
13 anterolateral aspect of the thigh or deltoid.

14

15 Do not administer this product intravenously, intradermally, or subcutaneously.

1

2 ActHIB vaccine should not be mixed in the same syringe with other parenteral products.

3

4 **3 DOSAGE FORMS AND STRENGTHS**

5 ActHIB vaccine is a solution for injection supplied as a single-dose vial of lyophilized powder to
6 be reconstituted with the supplied 0.4% Sodium Chloride diluent. A single dose, after
7 reconstitution is 0.5 mL.

8

9 **4 CONTRAINDICATIONS**

10 **4.1 Hypersensitivity**

11 Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any *H. influenzae* type b or
12 tetanus toxoid-containing vaccine or any component of the vaccine is a contraindication to
13 administration of ActHIB vaccine [see *Description (11)*].

14

15 **5 WARNINGS AND PRECAUTIONS**

16 **5.1 Management of Acute Allergic Reactions**

17 Epinephrine and other appropriate agents must be available should an acute anaphylactic reaction
18 occur.

19

20 **5.2 Guillain-Barré Syndrome**

1 If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior vaccine containing
2 tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including ActHIB
3 vaccine, should be based on careful consideration of the potential benefits and possible risks.
4

5 **5.3 Altered Immunocompetence**

6 In immunosuppressed persons, including those receiving immunosuppressive therapy, the
7 expected antibody responses may not be obtained.
8

9 **5.4 Limitations of Vaccine Effectiveness**

10 Vaccination with ActHIB vaccine may not protect 100% of individuals.
11

12 **5.5 Tetanus Immunization**

13 Immunization with ActHIB vaccine does not substitute for routine tetanus immunization.
14

15 **5.6 Interference with Laboratory Tests**

16 Urine antigen detection may not have a diagnostic value in suspected disease due to *H. influenzae*
17 type b within 1 to 2 weeks after receipt of a *H. influenzae* type b-containing vaccine, including
18 ActHIB [see *Drug Interactions (7.3)*].
19

1 **6 ADVERSE REACTIONS**

2 **6.1 Clinical Trials Experience**

3 Because clinical trials are conducted under widely varying conditions, adverse reaction rates
4 observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials
5 of another vaccine and may not reflect the rates observed in practice.

6

7 More than 7,000 infants and young children (≤ 2 years of age) have received at least one dose of
8 ActHIB vaccine during US clinical trials. Of these, 1,064 subjects 12 to 24 months of age who
9 received ActHIB vaccine alone reported no serious or life threatening adverse reactions.(1) (2)

10

11 Adverse reactions associated with ActHIB vaccine generally subsided after 24 hours and did not
12 persist beyond 48 hours after immunization.

13

14 In a US trial, the safety of ActHIB vaccine was evaluated in 110 children 15 to 20 months of age.
15 All children received three doses of *Haemophilus influenzae* type b conjugate vaccine (ActHIB
16 vaccine or a previously licensed Haemophilus b conjugate vaccine) at approximately 2, 4, and
17 6 months of age. The incidence of selected solicited injection site and systemic adverse reactions
18 which occurred within 48 hours following the dose of ActHIB vaccine is shown in **Table 1**.

19

20

1 **Table 1: Local and Systemic Reactions at 6, 24, and 48 Hours Following Immunization with**
2 **ActHIB Vaccine in Children 15 to 20 months old (2)**

| Adverse Event | 6 Hrs. Post-dose | 24 Hrs. Post-dose | 48 Hrs. Post-dose |
|----------------------------|------------------|-------------------|-------------------|
| Local (%) | N=110 | N=110 | N=110 |
| Tenderness | 20.0 | 8.2 | 0.9 |
| Erythema (>1") | 0.0 | 0.9 | 0.0 |
| Induration ^a | 5.5 | 3.6 | 0.9 |
| Swelling | 3.6 | 1.8 | 0.0 |
| Systemic (%) | N=103-110 | N=105-110 | N=104-110 |
| Fever (>102.2°F (>39.0°C)) | 0 | 1.0 | 1.9 |
| Irritability | 27.3 | 20.9 | 12.7 |
| Drowsiness | 36.4 | 17.3 | 12.7 |
| Anorexia | 12.7 | 10.0 | 6.4 |
| Vomiting | 0.9 | 0.9 | 0.9 |
| Persistent cry | 0 | 0 | 0 |
| Unusual cry | 0 | 0 | 0 |

3 ^a Induration is defined as hardness with or without swelling.

4
5 In a US clinical trial (P3T06), 1,454 children were enrolled and received one dose of ActHIB
6 vaccine at 2 months of age and subsequent doses administered at 4 and 6 months of age
7 (concomitantly with DAPTACEL® [a US-licensed diphtheria, tetanus and pertussis vaccine],
8 IPOL® [a US-licensed inactivated poliovirus vaccine] and PCV7 [Pneumococcal conjugate
9 vaccine, 7-valent]) vaccines at 2, 4, and 6 months of age and hepatitis B vaccine at 2 and
10 6 months of age). At 15-16 months of age, 418 children received a 4th dose of ActHIB and
11 DAPTACEL vaccines. The most frequent systemic reactions following any dose (>50% of
12 participants) were decreased activity/lethargy, fussiness/irritability, and inconsolable crying.

1 **Table 2: Number (Percentage) of Children with Selected Solicited Systemic Adverse**
2 **Reactions by Severity Occurring within 0-3 days After Vaccination in Study P3T06**

| Systemic Reactions | DAPTACEL + IPOL + ActHIB Vaccines | | | DAPTACEL + ActHIB Vaccines |
|--|-----------------------------------|------------------------------|------------------------------|----------------------------|
| | Dose 1 N=1,390-1,406 % | Dose 2 N=1,346-1,360 % | Dose 3 N=1,301-1,312 % | Dose 4 N=379-381 % |
| Fever^{ab} | | | | |
| ≥38.0°C | 9.3 | 16.1 | 15.8 | 8.7 |
| >38.5°C | 1.6 | 4.3 | 5.1 | 3.2 |
| >39.5°C | 0.1 | 0.4 | 0.3 | 0.8 |
| Decreased Activity/Lethargy^c | | | | |
| Any | 51.1 | 37.4 | 33.2 | 24.1 |
| Moderate or Severe | 24.3 | 15.8 | 12.7 | 9.2 |
| Severe | 1.2 | 1.4 | 0.6 | 0.3 |
| Inconsolable Crying | | | | |
| Any | 58.5 | 51.4 | 47.9 | 36.2 |
| ≥1 hour | 16.4 | 16.0 | 12.2 | 10.5 |
| >3 hours | 2.2 | 3.4 | 1.4 | 1.8 |
| Fussiness/Irritability | | | | |
| Any | 75.8 | 70.7 | 67.1 | 53.8 |
| ≥1 hour | 33.3 | 30.5 | 26.2 | 19.4 |
| >3 hours | 5.6 | 5.5 | 4.3 | 4.5 |

3 Note. - Ages of study participants ranged from 1.3 to 19.5 months.

4 ^a Fever is based upon actual temperatures recorded with no adjustments to the measurement route.

5 ^b Following Doses 1-3 combined, the proportion of temperature measurements that were taken by axillary, rectal or
6 other routes, or not recorded were 44.8%, 54.0%, 1.0%, and 0.1%. Following Dose 4, the proportion of temperature
7 measurements that were taken by axillary, rectal or other routes, or not recorded were 61.1%, 36.6%, 1.7%, and 0.5%.

8 ^c Moderate: interferes with or limits usual daily activity; Severe: disabling, not interested in usual daily activity.

9

10 In Study P3T06, within 30 days following any of Doses 1-3 of DAPTACEL + IPOL + ActHIB
11 vaccines, 50 of 1,455 (3.4%) participants experienced a serious adverse event (SAE). One SAE of
12 seizure with apnea occurring on the day of vaccination with the first dose of the three vaccines
13 was determined by the investigators as possibly related. Within 30 days following Dose 4, four of
14 418 (1.0%) participants who received DAPTACEL + ActHIB vaccines experienced a serious
15 adverse event. None was assessed by the investigators as related to the study of vaccines.

1

2 **6.2 Postmarketing Experience**

3 The following events have been spontaneously reported during the post-approval use of ActHIB
4 vaccine. Because these events are reported voluntarily from a population of uncertain size, it is
5 not always possible to reliably estimate their frequency or establish a causal relationship to
6 vaccine exposure.

7 • **Immune system disorders:**

8 Anaphylaxis, other allergic/hypersensitivity reactions (including urticaria, angioedema)

9 • **Nervous system disorders:**

10 Convulsions

11 • **General disorders and administration site conditions:**

12 Extensive limb swelling, peripheral edema, pruritus, rash

13

14 **7 DRUG INTERACTIONS**

15 **7.1 Concomitant Administration with Other Vaccines**

16 In clinical trials, ActHIB vaccine was administered, at separate sites, concomitantly with one or
17 more of the following vaccines: DTaP; Measles, Mumps and Rubella vaccine (MMR); Hepatitis
18 B vaccine; and Inactivated Poliovirus Vaccine (IPV). No impairment of the antibody response to
19 the individual antigens was demonstrated when ActHIB vaccine was given at the same time but
20 separate sites with these vaccines.(2)

21

22 **7.2 Immunosuppressive Treatments**

1 Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic
2 drugs, and corticosteroids (used in greater than physiologic doses) may reduce the immune
3 response to ActHIB vaccine [*see Altered Immunocompetence (5.3)*].
4

5 **7.3 Interference with Laboratory Tests**

6 Haemophilus b capsular polysaccharide derived from Haemophilus b Conjugate Vaccines has
7 been detected in the urine of some vaccinees. Urine antigen detection may not have a diagnostic
8 value in suspected disease due to *H. influenzae* type b within 1 to 2 weeks after receipt of a *H.*
9 *influenzae* type b-containing vaccine, including ActHIB [*see Warnings and Precautions (5.6)*].(3)
10

11 **8 USE IN SPECIFIC POPULATIONS**

12 **8.1 Pregnancy**

13 ActHIB is not approved for use in individuals 6 years of age and older. No human or animal data
14 are available to assess vaccine-associated risks in pregnancy.
15

16 **8.2 Lactation**

17 ActHIB is not approved for use in individuals 6 years of age and older. Human or animal data are
18 not available to assess the impact of ActHIB on milk production, its presence in breast milk, or its
19 effects on the breastfed infant.
20

21 **8.4 Pediatric Use**

1 Safety and effectiveness of ActHIB have not been established in infants below the age of 6 weeks
2 and children and adolescents 6 years of age and older [see *Dosage and Administration (2.1)*].

3

4 **11 DESCRIPTION**

5 ActHIB vaccine is a sterile, lyophilized powder to be reconstituted with saline diluent (0.4%
6 Sodium Chloride) for intramuscular administration only. The vaccine consists of the *Haemophilus*
7 *influenzae* type b capsular polysaccharide (polyribosyl-ribitol-phosphate, PRP), a high-molecular-
8 weight polymer prepared from the *H. influenzae* type b strain 1482 grown in a semi-synthetic
9 medium, covalently bound to tetanus toxoid. (4) The lyophilized ActHIB vaccine powder and
10 saline diluent contain no preservative. The tetanus toxoid is prepared by extraction, ammonium
11 sulfate purification, and formalin inactivation of the toxin from cultures of *Clostridium tetani*
12 (Harvard strain) grown in a modified Mueller and Miller medium. (5) The culture medium
13 contains milk-derived raw materials (casein derivatives). Further manufacturing process steps
14 reduce residual formaldehyde to levels below 0.5 micrograms (mcg) per dose by calculation. The
15 toxoid is filter sterilized prior to the conjugation process. Potency of ActHIB vaccine is specified
16 on each lot by limits on the content of PRP polysaccharide and protein in each dose and the
17 proportion of polysaccharide and protein in the vaccine that is characterized as high molecular
18 weight conjugate.

19

20 When ActHIB is reconstituted with saline diluent (0.4% Sodium Chloride), each 0.5-mL dose is
21 formulated to contain 10 mcg of purified capsular polysaccharide conjugated to 24 mcg of
22 inactivated tetanus toxoid and 8.5% of sucrose.

23 The vial stoppers for ActHIB vaccine and diluent are not made with natural rubber latex.

1

2 **12 CLINICAL PHARMACOLOGY**

3 **12.1 Mechanism of Action**

4 *Haemophilus influenzae* (*H. influenzae*) is a gram-negative coccobacillus. Most strains of *H.*
5 *influenzae* that cause invasive disease (e.g., sepsis and meningitis) are *H. influenzae* type b.

6

7 The response to ActHIB vaccine is typical of a T-dependent immune response to antigens. The
8 prominent isotype of anti-capsular PRP antibody induced by ActHIB vaccine is IgG. (6) A
9 booster response for IgG has been demonstrated in children 12 months of age or older who
10 previously received two or three doses of ActHIB vaccine. Bactericidal activity against *H.*
11 *influenzae* type b was demonstrated in serum after immunization and correlated with the anti-PRP
12 antibody response induced by ActHIB vaccine. (1)

13

14 Antibody titers to *H. influenzae* capsular polysaccharide (anti-PRP) of >1.0 mcg/mL following
15 vaccination with unconjugated PRP vaccine correlated with long-term protection against invasive
16 *H. influenzae* type b disease in children older than 24 months of age. (7) Although the relevance
17 of this threshold to clinical protection after immunization with conjugate vaccines is not known,
18 particularly in light of the induced, immunologic memory, this level continues to be considered as
19 indicative of long-term protection. (8) In clinical studies, ActHIB vaccine induced, on average,
20 anti-PRP levels ≥ 1.0 mcg/mL in 90% of infants after the primary series (2, 4, and 6 months) and
21 in more than 98% of infants following a booster dose given at 15 to 19 months of age. (1)

22

23 **13 NON-CLINICAL TOXICOLOGY**

1 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

2 ActHIB vaccine has not been evaluated for its carcinogenic or mutagenic potential or impairment
3 of male fertility.

4
5 **14 CLINICAL STUDIES**

6 **14.1 Immunogenicity of ActHIB Vaccine in Children 2, 4, and 6 Months of Age**

7 Two clinical trials supported by the National Institutes of Health (NIH) have compared the
8 anti-PRP antibody responses to three *Haemophilus influenzae* type b conjugate vaccines in
9 racially mixed populations of children. These studies were done in Tennessee (9) (Table 3) and in
10 Minnesota, Missouri, and Texas (10) (Table 4) in infants immunized with ActHIB vaccine and
11 other *Haemophilus influenzae* type b conjugate vaccines at 2, 4, and 6 months of age. All
12 *Haemophilus influenzae* type b conjugate vaccines were administered concomitantly with OPV
13 and whole-cell DTP vaccines at separate sites. Neither OPV nor whole-cell DTP vaccines are
14 licensed or distributed in the US currently.

15
16 **Table 3: Anti-PRP Antibody Responses Following a Two or Three Dose Series of a**
17 ***Haemophilus influenzae* type b Vaccine at 2, 4, and 6 Months of Age – Tennessee (9)**

| Vaccine | N ^a | Geometric Mean Concentration (GMC) (mcg/mL) | | | Post Third Immunization % ≥1.0 mcg/mL |
|--|----------------|--|--|---|--|
| | | Pre- Immunization at 2 months | Post Second Immunization at 6 months | Post Third Immunization at 7 months | |
| PRP-T ^b (ActHIB vaccine) | 65 | 0.10 | 0.30 | 3.64 | 83% |
| PRP-OMP ^c (PedvaxHIB®) | 64 | 0.11 | 0.84 | N/A | 50% ^d |
| HbOC ^e (HibTITER®) | 61 | 0.07 | 0.13 | 3.08 | 75% |

18 ^a N = Number of children

- 1 ^b *Haemophilus influenzae* type b Conjugate Vaccine (Tetanus Toxoid Conjugate)
 2 ^c *Haemophilus influenzae* type b Conjugate Vaccine (Meningococcal Protein Conjugate)
 3 ^d Seroconversion after the recommended 2-dose primary immunization series is shown
 4 ^e *Haemophilus influenzae* type b Conjugate Vaccine (Diphtheria CRM₁₉₇ Protein Conjugate)
 5 N/A = Not applicable in this comparison trial although third dose data have been published

6 **Table 4: Anti-PRP Antibody Responses Following a Two or Three Dose Series of a**
 7 ***Haemophilus influenzae* type b Vaccine at 2, 4, and 6 Months of Age - Minnesota, Missouri,**
 8 **and Texas (10)**

| Vaccine | N ^a | Geometric Mean Concentration (GMC) (mcg/mL) | | | Post Third ^b Immunization % ≥1.0 mcg/mL |
|--|----------------|--|--|--|---|
| | | Pre- Immunization at 2 months | Post Second Immunization at 6 months | Post Third ^b Immunization at 7 months | |
| PRP-T ^c (ActHIB vaccine) | 142 | 0.25 | 1.25 | 6.37 | 97% |
| PRP-OMP ^d (PedvaxHIB) | 149 | 0.18 | 4.00 | N/A | 85% ^e |
| HbOC ^f (HibTITER) | 167 | 0.17 | 0.45 | 6.31 | 90% |

- 9 ^a N = Number of children
 10 ^b Sera were obtained after the third dose from 86 and 110 infants, in PRP-T and HbOC vaccine groups, respectively
 11 ^c *Haemophilus influenzae* type b Conjugate Vaccine (Tetanus Toxoid Conjugate)
 12 ^d *Haemophilus influenzae* type b Conjugate Vaccine (Meningococcal Protein Conjugate)
 13 ^e Seroconversion after the recommended 2-dose primary immunization series is shown
 14 ^f *Haemophilus influenzae* type b Conjugate Vaccine (Diphtheria CRM₁₉₇ Protein Conjugate)
 15 N/A = Not applicable in this comparison trial although third dose data have been published (10)
 16

17 Native American populations have had high rates of *H. influenzae* type b disease and have been
 18 observed to have low immune responses to *Haemophilus influenzae* type b conjugate vaccines. In
 19 a clinical study enrolling Alaskan Native Americans, following the administration of a three-dose
 20 series of ActHIB vaccine at 6 weeks, 4 months, and 6 months of age, 75% of subjects achieved an
 21 anti-PRP antibody titer of ≥1.0 mcg/mL at 7 months of age (1 month after the last vaccination).
 22 (11)

1

2 **14.2 Immunogenicity of ActHIB Vaccine in Children 12 to 24 Months of Age**

3 In four separate studies, children 12 to 24 months of age who had not previously received
4 *Haemophilus influenzae* type b conjugate vaccination were immunized with a single dose of
5 ActHIB vaccine (**Table 5**). Geometric Mean Concentration (GMC) of anti-PRP antibody
6 responses were 5.12 mcg/mL (90% responding with ≥ 1.0 mcg/mL) for children 12 to 15 months
7 of age and 4.4 mcg/mL (82% responding with ≥ 1.0 mcg/mL) for children 17 to 24 months of age.
8 (2)

9 **Table 5: Anti-PRP Antibody Responses in 12- to 24-month-old Children Immunized with a**
10 **Single Dose of ActHIB**

| Age Group | N ^a | Geometric Mean Concentration (GMC) (mcg/mL) | | % Subjects With ≥ 1.0 mcg/mL | |
|-----------------|----------------|---|--------------------------------|-----------------------------------|--------------------------------|
| | | Pre-Immunization | Post-Immunization ^b | Pre-Immunization | Post-Immunization ^b |
| 12 to 15 months | 256 | 0.06 | 5.12 | 1.6 | 90.2 |
| 17 to 24 months | 81 | 0.10 | 4.40 | 3.7 | 81.5 |

11 ^a N = Number of children

12 ^b Post immunization responses measured at approximately 1 month after vaccination

13

14 ActHIB vaccine has been found to be immunogenic in children with sickle cell anemia, a
15 condition that may cause increased susceptibility to *Haemophilus influenzae* type b disease.

16 Following two doses of ActHIB vaccine given at two-month intervals, 89% of these children
17 (mean age 11 months) had anti-PRP antibody titers of ≥ 1.0 mcg/mL. This is comparable to

18 anti-PRP antibody levels demonstrated in normal children of similar age following two doses of
19 ActHIB vaccine. (12)

20

15 REFERENCES

- 1 Data on file, Sanofi Pasteur SA.
- 2
- 3 1 Data on file, Sanofi Pasteur Inc.
- 4 2 Rothstein EP, et al. Comparison of antigenuria after immunization with three Haemophilus
- 5 3 influenzae type b conjugate vaccines. *Pediatr Infect Dis J* 10:311-314, 1991.
- 6 4 Chu CY, et al. Further studies on the immunogenicity of Haemophilus influenzae type b and
- 7 5 pneumococcal type 6A polysaccharide-protein conjugate. *Infect Immun* 40:245-246, 1983.
- 8 6 Mueller JH, et al. Production of diphtheria toxin of high potency (100 Lf) on a reproducible
- 9 7 medium. *J Immunol* 40:21-32, 1941.
- 10 8 Holmes SJ, et al. Immunogenicity of four Haemophilus influenzae type b conjugate
- 11 9 vaccines in 17- to 19-month-old children. *J Pediatr* 118:364-371, 1991.
- 12 10 Peltola H, et al. Prevention of Haemophilus influenzae type b bacteremic infections with the
- 13 11 capsular polysaccharide vaccine. *N Engl J Med* 310:1561-1566, 1984.
- 14 12 Recommendations of the Immunization Practices Advisory Committee (ACIP).
- 15 13 Haemophilus b conjugate vaccines for prevention of Haemophilus influenzae type b disease
- 16 14 among infants and children two months of age and older. *MMWR* 40:No. RR-1, 1991.
- 17 15 Decker MD, et al. Comparative trial in infants of four conjugate Haemophilus influenzae
- 18 16 type b vaccines. *J Pediatr* 120:184-189, 1992.
- 19 17 Granoff DM, et al. Differences in the immunogenicity of three Haemophilus influenzae type
- 20 18 b conjugate vaccines in infants. *J Pediatr* 121:187-194, 1992.
- 21

- 1 11 Bulkow LR, et al. Comparative immunogenicity of four Haemophilus influenzae type b
2 conjugate vaccines in Alaska Native infants. *Pediatr Infect Dis J* 12:484-92, 1993.
- 3 12 Kaplan SL, et al. Immunogenicity of Haemophilus influenzae type b polysaccharide-tetanus
4 protein conjugate vaccine in children with sickle hemoglobinopathy or malignancies, and
5 after systemic Haemophilus influenzae type b infection. *J Pediatr* 120:367-370, 1992.
- 6 13 Vaccine Adverse Event Reporting System United States. *MMWR* 39:730-733, 1990.
- 7 14 CDC. National Childhood Vaccine Injury Act: Requirements for permanent vaccination
8 records and for reporting of selected events after vaccination. *MMWR* 37:197-200, 1988.
- 9 15 National Childhood Vaccine Injury Act of 1986 (Amended 1987).

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1 **16 HOW SUPPLIED/STORAGE AND HANDLING**

2 **16.1 How Supplied**

3 Single-dose, lyophilized vaccine vial (NDC 49281-547-58) packaged with single-dose diluent vial
4 (NDC 49281-546-58). Supplied as package of 5 vials each (NDC 49281-545-03).

5

6 The vial stoppers for ActHIB vaccine and diluent are not made with natural rubber latex.

7

8 **16.2 Storage and Handling**

9 Store lyophilized ActHIB vaccine packaged with saline diluent (0.4% Sodium Chloride) at 2° to
10 8°C (35° to 46°F). DO NOT FREEZE.

11

12 **17 PATIENT COUNSELING INFORMATION**

13 Vaccine Information Statements are required by the National Childhood Vaccine Injury Act of
14 1986 to be given prior to immunization to the patient, parent, or guardian.

15

16 Inform the patients, parents, or guardians about the potential benefits and risks of the vaccine and
17 importance of completing the immunization series unless a contraindication to further
18 immunization exists. In addition to this, parents and guardians must be informed about the
19 potential for adverse reactions that have been temporarily associated with the administration of
20 ActHIB vaccine or other vaccines containing similar ingredients. Prior to administration of
21 ActHIB vaccine, healthcare providers should ask parents or guardians about the recent health
22 status of the infant or child to be immunized. As part of the child's immunization record, the date,

1 lot number, and manufacturer of the vaccine administered should be recorded. (13) (14) (15)
2 Vaccine recipients and guardians must report any adverse reactions upon administration of the
3 vaccine to their healthcare provider and/or to the Vaccine Adverse Event Reporting System
4 (VAERS).

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7 ActHIB, DAPTACEL and IPOL are registered trademark of Sanofi Pasteur Inc.

8 PedvaxHIB® is a registered trademark of Merck & Co., Inc.

9 HibTITER® is a registered trademark of Nuron Biotech.

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Product information

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as of Month 201X.

13

14 Manufactured by:

15 **Sanofi Pasteur SA**

16 Marcy L'Etoile France

17

18 Distributed by:

19 **Sanofi Pasteur Inc.**

20 Swiftwater PA 18370 USA

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