INDICATIONS AND USAGE

Pentacel® is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis, polio and H. influenzae type b. Pentacel is approved for use as a four dose series in children 6 weeks through 4 years of age (prior to 5th birthday). (1)

The four dose immunization series consists of a 0.5 mL intramuscular injection, after reconstitution, administered at 2, 4, 6 and 15-18 months of age. (2.1)

Pentacel consists of a liquid vaccine component (DTaP-IPV component) and a lyophilized vaccine component (ActHIB vaccine). Reconstitute the ActHIB vaccine component with the DTaP-IPV component immediately before administration. (2.2)

DOSAGE AND ADMINISTRATION

Suspension for injection (0.5 mL dose) supplied as a liquid vaccine component that is combined through reconstitution with a lyophilized vaccine component, both in single-dose vials. (3)

- Severe allergic reaction (eg, anaphylaxis) after a previous dose of Pentacel, any ingredient of Pentacel, or any other diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, inactivated poliovirus vaccine or H. influenzae type b vaccine. (4.1)
- Encephalopathy within 7 days of a previous pertussis-containing vaccine with no other identifiable cause. (4.2)
- Progressive neurologic disorder until a treatment regimen has been established and the condition has stabilized. (4.3)

CONTRAINDICATIONS

WARNINGS AND PRECAUTIONS

- Carefully consider benefits and risks before administering Pentacel to persons with a history of:
  - fever ≥40.5°C (≥105°F), hypotonic-hyporesponsive episode (HHE) or persistent, inconstant crying lasting ≥3 hours within 48 hours after a previous pertussis-containing vaccine. (5.2)
  - seizures within 3 days after a previous pertussis-containing vaccine. (5.2)
- If Guillian-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the risk for Guillian-Barré syndrome may be increased following Pentacel. (5.3)
- For infants and children with a history of previous seizures, an anaphylactic or delayed systemic reaction or anaphylactic-like event following DTPa vaccination has occurred in <0.1% of participants, depending on dose number. Injection site reactions that occurred in ≥30% of participants following any dose included tenderness and increase in arm circumference. (6.1)

ADVERSE REACTIONS

- Rates of adverse reactions varied by dose number. Systemic reactions that occurred in >50% of participants following any dose included fussiness/irritability and inconstant crying. Fever ≥38.0°C occurred in ≥0.16% of participants, depending on dose number. Injection site reactions that occurred in ≥30% of participants following any dose included tenderness and increase in arm circumference. (6.1)

CONVERSE SEQUENCES:

- The decision about when to administer an intramuscular vaccine, including Pentacel, to infants born prematurely should be based on consideration of the individual infant’s medical status and the potential benefits and possible risks of vaccination. (5.7)

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 and http://vaers.hhs.gov.

- Do not mix Pentacel or any of its components with any other vaccine or diluent. (7.1)
- Immunosuppressive therapies may reduce the immune response to Pentacel. (7.2)
- Urine antigen detection may not have definitive diagnostic value in suspected H. influenzae type b disease within one week following Pentacel. (7.3)

See 17 for PATIENT COUNSELING INFORMATION

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*Sections or subsections omitted from the full prescribing information are not listed

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Mixed Sequences of Pentacel and DTaP Vaccine

While Pentacel and DAPTACEL® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed [DTaP], Sanofi Pasteur Limited) vaccines contain the same pertussis antigens, manufactured by the same process, Pentacel contains twice the amount of detoxified pertussis toxin (PT) and four times the amount of fimbriated hemagglutinin (PHA) as DAPTACEL®. Pentacel may be used to complete the first 4 doses of the 5-dose DTaP series in infants and children who have received 1 or more doses of DAPTACEL® and are also scheduled to receive the other antigens of Pentacel. However, data are not available on the safety and immunogenicity of such mixed sequences of Pentacel and DAPTACEL® for successive doses of the primary DTaP series. Children who have completed a 4-dose series with Pentacel should receive a fifth dose of DTaP vaccine using DAPTACEL® at 4-6 years of age. (1)

Data are not available on the safety and effectiveness of using mixed sequences of Pentacel and DTaP vaccine from different manufacturers.
Mixed Sequences of Pentacel and IPV Vaccine

Pentacel may be used in infants and children who have received 1 or more doses of another licensed IPV vaccine and are scheduled to receive the antigens of Pentacel. However, data are not available on the safety and immunogenicity of Pentacel in such infants and children. The Advisory Committee on Immunization Practices (ACIP) recommends that the final dose in the 4-dose IPV series be administered at age ≥4 years. (2) When Pentacel is administered at ages 2, 4, 6, and 15-18 months, an additional booster dose of IPV vaccine should be administered at age 4-6 years, resulting in a 5-dose IPV series. (2)

Mixed Sequences of Pentacel and Haemophilus b Conjugate Vaccine

Pentacel may be used to complete the vaccination series in infants and children previously vaccinated with one or more doses of Haemophilus b Conjugate Vaccine (either separately administered or as part of another combination vaccine), who are also scheduled to receive the other antigens of Pentacel. However, data are not available on the safety and immunogenicity of Pentacel in such infants and children. If different brands of Haemophilus b Conjugate Vaccines are administered to complete the series, three primary immunizing doses are needed, followed by a booster dose.

2.2 Administration

The package contains a vial of the DTaP-IPV component and a vial of lyophilized ActHIB vaccine component. After removing the “flip-off” caps, cleanse the DTaP-IPV and ActHIB vial stoppers with a suitable antiseptic. Using a sterile needle and syringe and aseptic technique, withdraw and administer a single 0.5-mL dose of Pentacel intramuscularly. Use a separate sterile needle and syringe for each injection. Charging needles between withdrawing the vaccine from the vial and injecting it into the recipient is not necessary unless the needle has been damaged or contaminated. Pentacel should be used immediately after reconstitution. Discard unused portion. Refer to Figures 1, 2, 3, 4, and 5.

Pentacel: Instructions for Reconstitution of ActHIB Vaccine Component with DTaP-IPV Component

In infants younger than 1 year, the anterolateral aspect of the thigh provides the largest muscle and is the preferred site of injection. In older children, the deltoid muscle is usually large enough for injection. The vaccine should not be injected into the gluteal area or areas where there may be a major nerve trunk.

Do not administer this product intravenously or subcutaneously. Pentacel should not be mixed in the same syringe with other parenteral products.

3 DOSAGE FORMS AND STRENGTHS

Pentacel is a suspension for injection (0.5 mL dose) supplied as a liquid vaccine component that is combined through reconstitution with a lyophilized vaccine component, both in single-dose vials. [See Dosage and Administration (2.2) and How Supplied/Storage and Handling (16)].

4 CONTRAINDICATIONS

4.1 Hypersensitivity

A severe allergic reaction (eg, anaphylaxis) after a previous dose of Pentacel or any other diphtheria toxoid, tetanus toxoid, or pertussis-containing vaccine, inactivated poliovirus vaccine or H. influenzae type b vaccine, or any ingredient of this vaccine is a contraindication to administration of Pentacel. [See Description (11)]

4.2 Encephalopathy

Encephalopathy (eg, coma, decreased level of consciousness, prolonged seizures) within 7 days of a previous dose of a pertussis containing vaccine that is not attributable to another identifiable cause is a contraindication to administration of any pertussis-containing vaccine, including Pentacel.

4.3 Progressive Neurologic Disorder

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy is a contraindication to administration of any pertussis-containing vaccine including Pentacel. Pertussis vaccine should not be administered to individuals with such conditions until a treatment regimen has been established and the condition has stabilized.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs.

5.2 Adverse Reactions Following Prior Pertussis Vaccination

If any of the following events occur within the specified period after administration of a pertussis vaccine, the decision to administer Pentacel should be based on careful consideration of potential benefits and possible risks.

- Temperature of ≥40.5°C (≥104.9°F) within 48 hours, not attributable to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode [HHE]) within 48 hours.
- Persistent, intractable crying lasting ≥3 hours within 48 hours.
- Seizures with or without fever within ≤3 days.

5.3 Guillain-Barré Syndrome and Brachial Neuritis

A review by the Institute of Medicine (IOM) found evidence for a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome. (3) If Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the risk for Guillain-Barré syndrome may be increased following Pentacel.

5.4 Infants and Children with a History of Previous Seizures

For infants or children with a history of previous seizures, an appropriate antiprylptic may be administered (in the dosage recommended in its prescribing information) at the time of vaccination with a vaccine containing acellular pertussis antigens (including Pentacel) and for the following 24 hours, to reduce the possibility of post-vaccination fever.

5.5 Limitations of Vaccine Effectiveness

Vaccination with Pentacel may not protect all individuals.

5.6 Altered Immunocompetence

If Pentacel is administered to immunocompromised persons, including persons receiving immunosuppressive therapy, the expected immune response may not be obtained. [See Drug Interactions (7.2)].

5.7 Apnea in Premature Infants

Apnea following intramuscular vaccination has been observed in some infants born prematurely. The decision about when to administer an intramuscular vaccine, including Pentacel, to an infant born prematurely should be based on consideration of the individual infant’s medical status and the potential benefits and possible risks of vaccination.

6 ADVERSE REACTIONS

6.1 Data from Clinical Studies

Rates of adverse reactions varied by dose number. The most frequent (>50% of participants) systemic reactions following any dose were fussiness/irritability and intractable crying. The most frequent (>30% of participants) injection site reactions following any dose were tenderness and increased circumference of the injected arm. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.

The safety of Pentacel was evaluated in four clinical studies in which a total of 5,980 participants received at least one dose of Pentacel. In three of the studies, conducted in the US, a total of 4,198 participants were enrolled to receive four consecutive doses of Pentacel. In the fourth study, conducted in Canada, 1,782 participants previously vaccinated with three doses of Pentacel received a fourth dose. The vaccination schedules of Pentacel, Control vaccines, and concomitantly administered vaccines used in these studies are provided in Table 1. Across the four studies, 55.8% of participants were female. Among participants in the three US studies, 64.5% were Caucasian, 9.2% were Black, 12.5% were Hispanic, 3.9% were Asian, and 9.5% were of other racial/ethnic groups. In the two controlled studies, the racial/ethnic distribution of participants who received Pentacel and Control vaccines was similar. In the Canadian fourth dose study, 86.0% of participants were Caucasian, 1.9% were Black, 0.8% were Hispanic, 4.3% were Asian, 2.0% were East Indian, 0.5% were Native Indian, and 4.5% were of other racial/ethnic groups.

Table 1: Clinical Safety Studies of Pentacel: Vaccination Schedules

<table>
<thead>
<tr>
<th>Study</th>
<th>Pentacel</th>
<th>Control Vaccines</th>
<th>Concomitantly Administered Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>494-01</td>
<td>2, 4, 6 and 15 months</td>
<td>HCPDT + POLIOVAX + ActHIB at 2, 4, 6, and 15 months</td>
<td>7-valent pneumococcal conjugate vaccine* (PCV7) at 2, 4, and 6 months; in a subset of participants† Hepatitis B vaccine at 2 and 6 months‡</td>
</tr>
<tr>
<td>P3T06</td>
<td>2, 4, 6, and 15-16 months</td>
<td>DARTCEL + IPOL + ActHIB at 2, 4, and 6 months; and DARTCEL + ActHIB at 15-16 months</td>
<td>PCV7* at 2, 4, and 6 months; Hepatitis B vaccine at 2 and 6 months‡</td>
</tr>
</tbody>
</table>
Table 1: Clinical Safety Studies of Pentacel: Vaccination Schedules (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Pentacel</th>
<th>Control Vaccines</th>
<th>Concomitantly Administered Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>494-03</td>
<td>2, 4, 6, and 15-16 months</td>
<td>None</td>
<td>PCV7 at 2, 4, and 6 months in all participants; and at 15 months in a random subset of participants</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatitis B vaccine at 2 and 6 months (if a dose was previously administered) or at 2, 4, and 8 months (if no previous dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Measles, mumps, rubella vaccine (MMR) and varicella vaccine at 12 or 15 months in random subsets of participants</td>
</tr>
<tr>
<td>5A9908</td>
<td>15-18 months</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HCPDT: non-US licensed DTaP vaccine that is identical to the DTaP component of Pentacel.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>POLIOVAX: US licensed Poliovirus Vaccine Inactivated, Sanofi Pasteur Limited.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IPOL: US licensed Poliovirus Vaccine Inactivated, Sanofi Pasteur SA.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*PCV7 manufactured by Wyeth Laboratories.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>†PCV7 was introduced after the study was initiated, and thus, administered concomitantly with Pentacel vaccine in a subset of participants.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>‡The first dose of hepatitis B vaccine (manufacturer not specified) was administered prior to study initiation, from birth to 21 days of age. Subsequent doses were with hepatitis B vaccine manufactured by Merck and Co.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>§MMR and varicella vaccines were both manufactured by Merck and Co.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>¶Study participants previously had received three doses of Pentacel vaccine by 8 months of age.</td>
</tr>
</tbody>
</table>

Solicited Adverse Reactions
The incidence and severity of selected solicited injection site and systemic adverse reactions that occurred within 3 days following each dose of Pentacel or Control vaccines in Study P3T06 is shown in Table 2. Information on these reactions was recorded daily by parents or guardians on diary cards. In Table 2, injection site reactions are reported for the Pentacel and DAPTACEL injection sites.

Table 2: Number (Percentage) of Children with Selected Solicited Adverse Reactions by Severity Occurring within 0-3 days of Pentacel or Control Vaccines in Study P3T06

<table>
<thead>
<tr>
<th>Injection Site Reactions</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td>7.1</td>
<td>8.4</td>
<td>8.7</td>
<td>17.3</td>
</tr>
<tr>
<td>&gt;25 mm</td>
<td>2.8</td>
<td>1.8</td>
<td>1.8</td>
<td>9.2</td>
</tr>
<tr>
<td>&gt;50 mm</td>
<td>0.6</td>
<td>0.2</td>
<td>0.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Swelling</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td>7.5</td>
<td>7.3</td>
<td>5.0</td>
<td>9.7</td>
</tr>
<tr>
<td>&gt;25 mm</td>
<td>3.0</td>
<td>2.0</td>
<td>1.6</td>
<td>3.8</td>
</tr>
<tr>
<td>&gt;50 mm</td>
<td>0.9</td>
<td>0.0</td>
<td>0.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Tenderness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>47.5</td>
<td>39.2</td>
<td>42.7</td>
<td>56.1</td>
</tr>
<tr>
<td>Moderate or Severe</td>
<td>19.6</td>
<td>10.6</td>
<td>11.6</td>
<td>16.7</td>
</tr>
<tr>
<td>Severe</td>
<td>5.4</td>
<td>1.6</td>
<td>1.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Increase in Arm Circumference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td></td>
<td></td>
<td></td>
<td>33.6</td>
</tr>
<tr>
<td>&gt;20 mm</td>
<td></td>
<td></td>
<td></td>
<td>4.7</td>
</tr>
<tr>
<td>&gt;40 mm</td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Systemic Reactions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥38.0°C</td>
<td>5.8</td>
<td>10.9</td>
<td>16.3</td>
<td>13.4</td>
</tr>
<tr>
<td>&gt;38.5°C</td>
<td>1.3</td>
<td>2.4</td>
<td>4.4</td>
<td>5.1</td>
</tr>
<tr>
<td>&gt;39.5°C</td>
<td>0.4</td>
<td>0.0</td>
<td>0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Decreased Activity/Lethargy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>46.8</td>
<td>32.7</td>
<td>32.5</td>
<td>24.1</td>
</tr>
<tr>
<td>Moderate or Severe</td>
<td>22.9</td>
<td>12.4</td>
<td>12.7</td>
<td>9.8</td>
</tr>
<tr>
<td>Severe</td>
<td>2.1</td>
<td>0.7</td>
<td>0.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Inconsolable Crying</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>59.3</td>
<td>49.8</td>
<td>47.3</td>
<td>35.9</td>
</tr>
<tr>
<td>≥1 hour</td>
<td>19.7</td>
<td>10.6</td>
<td>13.6</td>
<td>11.8</td>
</tr>
<tr>
<td>&gt;3 hours</td>
<td>1.9</td>
<td>0.9</td>
<td>1.1</td>
<td>2.3</td>
</tr>
</tbody>
</table>

HCPDT: non-US licensed DTaP vaccine that is identical to the DTaP component of Pentacel. POLIOVAX: US licensed Poliovirus Vaccine Inactivated, Sanofi Pasteur Limited. IPOL: US licensed Poliovirus Vaccine Inactivated, Sanofi Pasteur SA. *PCV7 manufactured by Wyeth Laboratories. †PCV7 was introduced after the study was initiated, and thus, administered concomitantly with Pentacel vaccine in a subset of participants. ‡The first dose of hepatitis B vaccine (manufacturer not specified) was administered prior to study initiation, from birth to 21 days of age. Subsequent doses were with hepatitis B vaccine manufactured by Merck and Co. §MMR and varicella vaccines were both manufactured by Merck and Co. ¶Study participants previously had received three doses of Pentacel vaccine by 8 months of age.
Hypotonic Hyporesponsive Episodes

In Study P3T06, the diary cards included questions pertaining to HHEs. In Studies 494-01, 494-03, and SA9098, a question about the occurrence of fainting or change in mental status was asked during post-vaccination phone calls. HHEs, assessed in a report of a US Public Health Service workshop (4) were reported among participants who received Pentacel (N = 5,979), separately administered HCPDT + POLIOVAX + ActHIB (N = 1,032) or separately administered DAPTACEL + IPOL + ActHIB (N = 1,455). Hypotonia not fulfilling HHE criteria within 7 days following vaccination was reported in 4 participants after the administration of Pentacel (on the same day as the 1st dose, 3 on the same day as the 3rd dose) and in 1 participant after the administration of DAPTACEL + IPOL + ActHIB (4 days following the 1st dose).

Seizures

Across Studies 494-01, 494-03, SA9098 and P3T06, a total of 8 participants experienced a seizure within 7 days following either Pentacel (4 participants, N = 4,197 for at least one of Doses 1-3; N = 5,033 for Dose 4), separately administered HCPDT + POLIOVAX + ActHIB (3 participants, N = 1,032 for at least one of Doses 1-3, N = 739 for Dose 4), or separately administrated DAPTACEL + IPOL + ActHIB (1 participant; N = 1,455 for at least one of Doses 1-3), or separately administrated DAPTACEL + ActHIB (0 participants; N = 418 for Dose 4). Among the four participants who experienced a seizure within 7 days following Pentacel, one participant in Study 494-01 had an afebrile seizure 6 days after the first dose, one participant had a febrile seizure the same day as the third dose and two participants in Study SA9098 had a febrile seizure 2 and 4 days, respectively, after the fourth dose. Among the four participants who experienced a seizure within 7 days following Control vaccines, one participant had an afebrile seizure the same day as the first dose of DAPTACEL + IPOL + ActHIB, one participant had an afebrile seizure the same day as the second dose of HCPDT + POLIOVAX + ActHIB and two participants had a febrile seizure 6 and 7 days, respectively, after the fourth dose of HCPDT + POLIOVAX + ActHIB.

Serious Adverse Events

In Study P3T06, within 30 days following any of Doses 1-3 of Pentacel or Control vaccines, 19 of 484 (3.9%) participants who received Pentacel and 50 of 1,435 (3.5%) participants who received DAPTACEL + IPOL + ActHIB experienced a serious adverse event. Within 30 days following Dose 4 of Pentacel or Control vaccines, 5 of 431 (1.2%) participants who received Pentacel and 4 of 418 (1.0%) participants who received DAPTACEL + IPOL + ActHIB experienced a serious adverse event. In Study 494-01, within 30 days following any of Doses 1-3 of Pentacel or Control vaccines, 23 of 2,506 (0.9%) participants who received Pentacel and 11 of 1,032 (1.1%) participants who received HCPDT + POLIOVAX + ActHIB experienced a serious adverse event. Within 30 days following Dose 4 of Pentacel or Control vaccines, 6 of 1,262 (0.5%) participants who received Pentacel and 2 of 739 (0.3%) participants who received HCPDT + POLIOVAX + ActHIB experienced a serious adverse event.

Across Studies 494-01, 494-03 and P3T06, within 30 days following any of Doses 1-3 of Pentacel or Control vaccines, overall, the most frequently reported serious adverse events were bronchitis, dehydration, pneumonia and gastroenteritis. Across Studies 494-01, 494-03, SA9098 and P3T06, within 30 days following Dose 4 of Pentacel or Control vaccines, overall, the most frequently reported serious adverse events were dehydration, gastroenteritis, asthma, and pneumonia.

Across Studies 494-01, 494-03, SA9098 and P3T06, two cases of encephalopathy were reported, both in participants who had received Pentacel (N = 5,979). One case occurred 30 days post-vaccination and was secondary to cardiac arrest following cardiac surgery. One infant who had onset of neurologic symptoms 8 days post-vaccination was subsequently found to have structural cerebral abnormalities and was diagnosed with congenital encephalopathy. A total of 5 deaths occurred during Studies 494-01, 494-03, SA9098 and P3T06: 4 in children who had received Pentacel (N = 5,979) and one in a participant who had received DAPTACEL + IPOL + ActHIB (N = 1,455). There were no deaths reported in children who received HCPDT + POLIOVAX + ActHIB (N = 1,032). Causes of death among children who received Pentacel were asphyxia due to suffocation, head trauma, Sudden Infant Death syndrome, and neutropenia (8, 23, 52 and 256 days post-vaccination, respectively). One participant with epidermolysis died secondary to aspiration 222 days following DAPTACEL + IPOL + ActHIB.

6.2 Data from Postmarketing Experience

The following additional adverse events have been spontaneously reported during the post-marketing use of Pentacel worldwide, since 1997. Between 1997 and 2007, Pentacel was primarily used in Canada. Because these events are reported voluntarily from a population of uncertain size, it may not be possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. The following adverse events were included based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to Pentacel.

- **Cardiac disorders**
  - Cyanosis
  - Gastrointestinal disorders
  - Vomiting, diarrhea
  - General disorders and administration site conditions
  - Injection site reactions (including inflammation, mass, abscess and sterile abscess), extensive swelling of the injected limb (including swelling that involved adjacent joints), vaccination failure/therapeutic response decreased (invasive H. influenzae type b disease)

- **Immunize system disorders**
  - Anaphylaxis/anaphylactic reaction, hypersensitivity (such as rash and urticaria)

- **Infections and infestations**
  - Meningitis, encephalitis, viral infection

- **Metabolism and nutrition disorders**
  - Decreased appetite

- **Nervous system disorders**
  - Somnolence, HHE, depressed level of consciousness

- **Psychiatric disorders**
  - Sinking

- **Respiratory, thoracic and mediastinal disorders**
  - Apnea, cough

- **Skin and subcutaneous tissue disorders**
  - Erythema, skin discoloration

- **Vascular disorders**
  - Tailor

7. DRUG INTERACTIONS

7.1 Concomitant Administration with Other Vaccines

In clinical trials, Pentacel was administered concomitantly with one or more of the following US licensed vaccines: hepatitis B vaccine, 7-valent pneumococcal conjugate vaccine, MMR and varicella vaccines. [See Adverse Reactions (8) and Clinical Studies (14)] When Pentacel is given at the same time as another injectable vaccine(s), the vaccine(s) should be administered with different syringes and at different injection sites.

7.2 Immunosuppressive Treatments

Immunosuppressive therapies, including irradiation, antimitobal agents, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to Pentacel. [See Warnings and Precautions (2.6)].

7.3 Drug/Laboratory Test Interactions

Antigenuria has been detected in some instances following receipt of ActHib. Urine antigen detection may not have definite diagnostic value in suspected H. influenzae type b disease within one week following receipt of Pentacel. [5]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pentacel is not approved for use in individuals 5 years of age and older. No human or animal data are available to assess vaccine-associated risks in pregnancy.

8.2 Lactation

Pentacel is not approved for use in individuals 5 years of age and older. No human or animal data are available to assess the impact of Pentacel on milk production, its presence in breast milk, or its effects on the breastfed infant.

8.4 Pediatric Use

The safety and effectiveness of Pentacel was established in the age group 19 months through 4 years in four clinical studies. [See Adverse Reactions (6.1) and Clinical Studies (14)] The safety and effectiveness of Pentacel in the age group 19 months through 4 years is supported by evidence in

8.11 DESCRIPTION

Pentacel consists of a Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Polioviruses [Type 1, 2, and 3 (Sabin strains) and Type b disease (type b disease)] and Haemophilus b Conjugate Vaccine [Tetanus T oxoid Conjugate], consists of H. influenzae type b capsular polysaccharide (polyribosyl-ribitol-phosphate [PRP]) covalently bound to tetanus toxoid (PRP-T). The DTaP-IPV component is supplied as a sterile liquid used to reconstitute the lyophilized ActHIB component to form Pentacel. Pentacel is a uniform, cloudy, white to off-white (yellow tinge) suspension.

4.5 mL of Pentacel contains 15 Lf diphtheria toxoid, 5 Lf tetanus toxoid, 20 mg acellular pertussis antigens [20 mcg pertussis toxin (PT), 20 mcg filamentous hemagglutinin (FHA), 3 mcg pertactin (PRN), 5 mcg fimbriae types 2 and 3 (FIM)], inactivated polioviruses [40 D-antigen units (DU) Type 1 (Mahoney), 8 DU Type 2 (MEF-1), 32 DU Type 3 (Saukett) and 10 mcg PRP of H. influenzae type b covalently bound to 24 mcg of tetanus toxin (PPP-T)]. Other ingredients per 0.5 mL dose contain 1.5 mg aluminium phosphate (0.33 mg aluminium) as the adjuvant, polysorbate 80 (approximately 10 ppm by calculation), 42.5 mg sucrose, <2 mcg residual formaldehyde, <0.50 ng residual glutaraldehyde, <0.50 ng residual bovine serum albumin, 3.3 mg (0.6% w/v) 2-phenoxethanol (not as a preservative), <4 pg of neomycin and <4 pg polynycin B sulphate. Corynebacterium diphtheriae is grown in modified Mueller’s growth medium. (6) After purification by ammonium sulfate fractionation, the diphtheria toxin is detoxified with formaldehyde and dialyzed. Cholera toxin is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulfate fractionation and dialyis. Diphtheria and tetanus toxoids are individually adsorbed onto aluminium phosphate.
The acellular pertussis vaccine antigens are produced from Bordetella pertussis cultures grown in Stainer-Scholte medium (8) modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. PT, FHA and PRN are isolated separately from the supernatant culture medium. FIM are extracted and copurified from the bacterial cells. The pertussis antigens are purified by sequential filtration, salt-precipitation, ultrafiltration and chromatography. PT is detoxified with glutaraldehyde. FHA is treated with formaldimethane and the residual aldehydes are removed by ultrafiltration. The individual antigens are adsorbed separately onto aluminum phosphate. Poliovirus Type 1, Type 2 and Type 3 are each grown in separate cultures of MR-5-6 cells, a line of normal human diploid cells, by the microcarrier method. (9) (10) The cells are grown in CCMRL (Connaught Medical Research Laboratories) 1969 medium, supplemented with calf serum. For viral growth, the culture medium is replaced by Medium 199, without calf serum. After clarification and filtration, the viral suspensions are concentrated by ultrafiltration, and purified by liquid chromatography steps. The monoclonal viral suspensions are inactivated with formaldimethane. Monovalent concentrates of each inactivated poliovirus are combined to produce a trivalent poliovirus concentrate. Polioviruses, of which there are three serotypes (Types 1, 2, and 3) are enteroviruses. The presence of poliovirus type-specific neutralizing antibodies has been correlated with protection against poliomyelitis. (16) Tetanus is an acute disease caused by an extremely potent neurotoxin produced by Clostridium tetani. Protection against disease is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of 0.1 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. (13) Levels of 1.0 IU/mL have been associated with long-term protection. (14)

12 CLINICAL PHARMACOLOGY

12.1 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 at least 0.1 IU/mL and 1.0 IU/mL have been associated with long-term protection. (14)

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 at least 0.01 IU/mL determined by neutralization assay is considered the minimum protective level. (13) (15) A tetanus antitoxin level ≥ 0.1 IU/mL as measured by the ELISA used in clinical studies of Pentacel is considered protective.

Pertussis

Pertussis (whooping cough) is a respiratory disease caused by B. pertussis. This Gram-negative cocobacillus 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

Poliomyelitis, of which there are three serotypes (Types 1, 2, and 3) are enteroviruses. The presence of poliovirus type-specific neutralizing antibodies has been correlated with protection against poliomyelitis. (16)

Invasive Disease Due to H. influenzae Type b

H. influenzae type b can cause invasive disease such as meningitis and sepsis. 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 (17) and an efficacy study with H. influenzae type b polysaccharide vaccine in Finland, (18) a post-vaccination anti-PRP level of 0.15 mcg/mL has been accepted as a minimal protective level. Data from an efficacy study with H. influenzae type b polysaccharide vaccine in Finland indicate that a level >1.0 mcg/mL, 3 weeks after vaccination protects against a subsequent one-year period. (19) (20) These levels have been used to evaluate the effectiveness of Haemophilus b Conjugate Vaccines, including the ActHIB component of Pentacel.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Pentacel has not been evaluated for carcinogenic or mutagenic potential or impairment of fertility.

14 CLINICAL STUDIES

The efficacy of Pentacel is based on the immunogenicity of the individual antigens compared to separately administered vaccines. Serological correlates of protection exist for diphtheria, tetanus, poliomyelitis, and invasive disease due to H. influenzae type b. [See Clinical Pharmacology (12.1).] The efficacy against pertussis, for which there is no well established serological correlate of protection, was based, in part, on a companion of pertussis immune responses following Pentacel in US children to responses following DAPTACEL (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) manufactured by Sanofi Pasteur Limited) in an efficacy study conducted in Sweden (Sweden I Efficacy Trial). Pentacel and DAPTACEL contain the same pertussis antigens, manufactured by the same process, Pentacel contains twice as much detoxified PT and four times as much FHA as DAPTACEL. Immune responses to Pentacel were evaluated in four LG studies: Studies 494-01, P3T06, 494-03, and MS 150584-04. The administration schedules of Pentacel, Control vaccine, and concomitantly administered vaccines used in Studies 494-01, P3T06, and 494-03 are provided in Table 1. (See Adverse Reactions (6.1)). In Study MS100, participants were randomized to receive Pentacel or separately administered DAPTACE, IPOL, and ActHIB at 2, 4, and 6 months of age. 7-valent pneumococcal conjugate (PCV7, Wyeth Pharmaceuticals Inc.) at 2, 4, and 6 months of age, and Hepatitis B vaccine (Merck and Co. or GlaxoSmithKline Biologies) at 2 and 6 months of age, were administered concomitantly with Pentacel or Control vaccines.

14.1 Diphtheria

The proportions of participants achieving diphtheria antitoxin seroprotective levels one month following three and four doses of Pentacel or DAPTACEL in Study P3T06 are provided in Table 3. The proportions of participants achieving diphtheria antitoxin seroprotective levels one month following three and four doses of Pentacel or DAPTACEL in Study P3T06 are provided in Table 3.

14.2 Tetanus

The proportions of participants achieving tetanus antitoxoid seroprotective levels one month following three and four doses of Pentacel or DAPTACEL in Study P3T06 are provided in Table 3.

Table 3: Study P3T06 Diphtheria Antitoxin and Tetanus Antitoxoid Responses One Month Following Dose 3 and Dose 4 of Pentacel or DAPTACEL + IPOL + ActHIB in US Children Vaccinated at 2, 4, 6, and 15-16 Months of Age

<table>
<thead>
<tr>
<th></th>
<th>Pentacel</th>
<th>DAPTACEL + IPOL + ActHIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-Dose 3</td>
<td>N = 331-345</td>
<td>N = 1,037-1,099</td>
</tr>
<tr>
<td>Diphtheria Antitoxin</td>
<td>% ≥ 0.01 IU/mL</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% ≥ 0.10 IU/mL</td>
<td>98.6%</td>
</tr>
<tr>
<td></td>
<td>% ≥ 1.0 IU/mL</td>
<td>98.5%</td>
</tr>
<tr>
<td>Tetanus Antitoxoid</td>
<td>% ≥ 0.10 IU/mL</td>
<td>99.4%</td>
</tr>
<tr>
<td>Post-Dose 4</td>
<td>N = 341-352</td>
<td>N = 328-334</td>
</tr>
<tr>
<td>Diphtheria Antitoxin</td>
<td>% ≥ 0.10 IU/mL</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% ≥ 0.10 IU/mL</td>
<td>96.5%</td>
</tr>
<tr>
<td></td>
<td>% ≥ 1.0 IU/mL</td>
<td>95.7%</td>
</tr>
<tr>
<td>Tetanus Antitoxoid</td>
<td>% ≥ 0.10 IU/mL</td>
<td>100.0%</td>
</tr>
<tr>
<td></td>
<td>% ≥ 0.10 IU/mL</td>
<td>92.4%</td>
</tr>
</tbody>
</table>

Per Protocol Immunogenicity population.

*Seroprotection rate following Pentacel vaccine is not inferior to DAPTACEL vaccine (upper limit of 95% CI of the difference DAPTACEL – Pentacel = <10%).

†Non-inferiority criteria were not pre-specified.

‡With the ELISA used in this study, a tetanus antitoxoid level of 1.0 IU/mL is 10 times the protective level.

Based on comparison of the immune responses to DAPTACEL in US infants (Post-Dose 3) and Canadian children (Post-Dose 4) relative to infants who participated in the Sweden I Efficacy Trial, it was concluded that 4 doses of DAPTACEL were needed for primary immunization against pertussis in US children. (1)

In a serology bridging analysis, immune responses to FHA, PRN and FIM in a subset of infants who received 3 doses of DAPTACEL in the Sweden I Efficacy Trial were compared to the Post-Dose 3 and Post-Dose 4 responses in a subset of US children from Study 494-01 who received Pentacel (Table 4). Available stored sera from infants who received DAPTACEL in the Sweden I Efficacy Trial and sera from children who received PCV7 concomitantly with the first three doses of Pentacel in Study 494-01 (Table 1) were assayed in parallel. Data on levels of antibody to PT using an adequately specific assay were not available for this serology bridging analysis.

Geometric mean antibody concentrations (GMACs) and seroconversion rates for antibodies to FHA, PRN and FIM one month following Dose 3 of DAPTACEL in the subset of infants from the Sweden I Efficacy Trial and one month following Dose 3 and Dose 4 of Pentacel in a subset of infants from US Study 494-01 are presented in Table 4. Seroconversion was defined as a 4-fold rise in antibody level (Post-Dose 3/Pre-Dose 1 or Post-Dose 4/Pre-Dose 1). For anti-FHA, anti-PRN, and anti-FIM, the non-inferiority criteria were met for GMACs, following Dose 4 of Pentacel relative to Dose 3 of DAPTACEL. The non-inferiority criterion for anti-PRN seroconversion following Dose 4 of Pentacel relative to Dose 3 of DAPTACEL was not met (upper limit of 95% CI for difference in rate (DAPTACEL minus Pentacel) = 13.24%). Whether the lower anti-PRN seroconversion rate following Dose 4 of Pentacel in US children relative to Dose 3 of DAPTACEL in Swedish infants correlates with diminished efficacy of Pentacel against pertussis is unknown.
### Table 4: FHA, PRN and FIM Antibody Responses One Month Following Dose 3 of DAPTACEL in a Subset of Infants Vaccinated at 2, 4, and 6 Months of Age in the Sweden I Efficacy Trial and One Month Following Dose 3 and Dose 4 of Pentacel in a Subset of Infants Vaccinated at 2, 4, 6, and 15-16 Months of Age in US Study 494-01

<table>
<thead>
<tr>
<th>Group</th>
<th>Post-Dose 3 DAPTACEL</th>
<th>Post-Dose 3 Pentacel US Study 494-01</th>
<th>Post-Dose 4 Pentacel US Study 494-01</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>80</td>
<td>730-995</td>
<td>507-564</td>
</tr>
</tbody>
</table>

- **Anti-FHA** % achieving 4-fold rise
  - GMC (EU/mL): 68.8
  - 40.70

- **Anti-PRN** % achieving 4-fold rise
  - GMC (EU/mL): 98.8
  - 111.26

- **Anti-FIM** % achieving 4-fold rise
  - GMC (EU/mL): 86.3
  - 339.31

---

### Table 5: Pertussis Antibody Responses One Month Following Doses 3 and 4 of Pentacel or DAPTACEL + IPOL + ActHIB in US Infants Vaccinated at 2, 4, 6, and 15-16 Months of Age in Study P3T06 (continued)

<table>
<thead>
<tr>
<th>Group</th>
<th>Post-Dose 3 Pentacel</th>
<th>Post-Dose 3 DAPTACEL + IPOL + ActHIB</th>
<th>Post-Dose 4 Pentacel</th>
<th>Post-Dose 4 DAPTACEL + IPOL + ActHIB</th>
</tr>
</thead>
</table>
| Anti-FIM    | % achieving 4-fold rise
  - GMC (EU/mL): 2.29
  - 553.30
| Anti-PRP    | % achieving 4-fold rise
  - GMC (EU/mL): 6.23
  - 6.23
| Anti-FIM    | % achieving 4-fold rise
  - GMC (EU/mL): 2.22
  - 2.29

### Table 6: Anti-PRP Seroprotection Rates and GMCs One Month Following Three Doses of Pentacel or Separate DTaP + IPOL + ActHIB Administered at 2, 4, and 6 Months of Age in Studies 494-01, P3T06, and MSA10

<table>
<thead>
<tr>
<th>Group</th>
<th>Anti-PRP % achieving ≥ 1.0 mcg/mL</th>
<th>Anti-PRP % achieving ≥ 0.15 mcg/mL</th>
<th>Anti-PRP GMC (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 494-01</td>
<td>Pentacel</td>
<td>HCPDT + POLIOVAX + ActHIB</td>
<td>N = 401</td>
</tr>
<tr>
<td>N = 1,127</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% achieving anti-PRP ≥ 0.15 mcg/mL</td>
<td>95.42%</td>
<td>98.3%</td>
<td></td>
</tr>
<tr>
<td>% achieving anti-PRP ≥ 1.0 mcg/mL</td>
<td>79.14%</td>
<td>88.8%</td>
<td></td>
</tr>
<tr>
<td>Anti-PRP GMC (mcg/mL)</td>
<td>3.197</td>
<td>6.23</td>
<td></td>
</tr>
</tbody>
</table>

| Study P3T06 | Pentacel                         | HCPDT + POLIOVAX + ActHIB         | N = 1,128              |
| N = 365     |                                  |                                   |                       |
| % achieving anti-PRP ≥ 0.15 mcg/mL | 92.39%                           | 93.3%                            |
| % achieving anti-PRP ≥ 1.0 mcg/mL  | 71.53%                           | 70.8%                            |
| Anti-PRP GMC (mcg/mL)                 | 2.316                            | 2.29                             |
Table 6: Anti-PRP Seroprotection Rates and GMCs One Month Following Three Doses of Pentacel or Separate DTaP + IPV + ActHIB Administered at 2, 4, and 6 Months of Age in Studies 494-01, P3T06, and MA510 (continued)

<table>
<thead>
<tr>
<th>Study MA510</th>
<th>Pentacel N = 826</th>
<th>DAPTACE + IPOL + ActHIB N = 421</th>
</tr>
</thead>
<tbody>
<tr>
<td>% achieving anti-PRP ≥0.15 mcg/mL</td>
<td>93.8%</td>
<td>90.3%</td>
</tr>
<tr>
<td>% achieving anti-PRP ≥1.0 mcg/mL</td>
<td>75.1%</td>
<td>74.8%</td>
</tr>
<tr>
<td>Anti-PRP GMC (mcg/mL)</td>
<td>2.52x</td>
<td>2.38</td>
</tr>
</tbody>
</table>

Per Protocol Immunogenicity population for all studies.

*Percent achieving specified level following Pentacel vaccine not inferior to ActHIB vaccine [upper limit of 90% CI for difference in rates (ActHIB minus Pentacel) <10%].

†Non-inferiority criterion not met for percent achieving anti-PRP ≥1.0 mcg/mL following Pentacel vaccine relative to ActHIB vaccine [upper 90% CI for difference in rates (ActHIB minus Pentacel) 12.9%, exceeds the non-inferiority criterion <10%].

‡Non-inferiority criterion not met for GMC following Pentacel vaccine relative to ActHIB vaccine [upper 90% CI for difference in rates (ActHIB minus Pentacel) 12.9%, exceeds the non-inferiority criterion <1.5].

§Non-inferiority criterion not pre-specified.

¶Percent achieving specified level following Pentacel vaccine not inferior to ActHIB vaccine [upper limit of 95% CI for difference in rates (ActHIB minus Pentacel) <10%].

\(*\)GMC following Pentacel vaccine not inferior to ActHIB vaccine [upper limit of 90% CI of GMC ratio (ActHIB/Pentacel) <1.5].

In Study 494-01, at 15 months of age prior to receipt of Dose 4 of study vaccines, 66.6% of Pentacel recipients (N = 829) and 80.6% of separately administered ActHIB recipients (N = 291) had an anti-PRP level ≥0.15 mcg/mL. Following Dose 4 of study vaccines, 92.8% of Pentacel recipients (N = 874) and 99.0% of separately administered ActHIB recipients (N = 231) had an anti-PRP level ≥1.0 mcg/mL.

In Study P3T06, at 15 months of age prior to receipt of Dose 4 of study vaccines, 65.4% of Pentacel recipients (N = 335) and 60.7% of separately administered ActHIB recipients (N = 323) had an anti-PRP level ≥0.15 mcg/mL. Following Dose 4 of study vaccines, 97.8% of Pentacel recipients (N = 361) and 95.9% of separately administered ActHIB recipients (N = 340) had an anti-PRP level ≥1.0 mcg/mL.

14.6 Concomitantly Administered Vaccines

In Study P3T06, (Table 1) there was no evidence for reduced antibody responses to hepatitis B vaccine (percent of participants with anti-HBs ≥10 mIU/mL) and GMCs to each serotype) administered concomitantly with Pentacel (N = 321-325) relative to these vaccines administered concomitantly with DAPTACE + IPOL + ActHIB (N = 996-1,029). The immune response to hepatitis B vaccine and PCV7 were evaluated one month following the third dose. In Study 494-03, (Table 1) there was no evidence for interference in the immune response to the fourth dose of PCV7 (percent of participants with antibody levels ≥0.15 mcg/mL and ≥0.5 mcg/mL and GMCs) or each serotype) administered concomitantly with Pentacel (N = 155) relative to this vaccine administered concomitantly with MMR and varicella vaccines (N = 158). There was no evidence for interference in the immune response to MMR and varicella vaccines (percent of participants with pre-specified seroresponse level) administered at 15 months of age concomitantly with Pentacel (N = 154) relative to these vaccines administered concomitantly with PCV7 (N = 144). The immune responses to MMR, varicella vaccine and the fourth dose of PCV7 were evaluated one month post-vaccination.

15 REFERENCES

1. DAPTACE® [full prescribing information]. Toronto, ON: Sanofi Pastuer; 2016.


16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

The vial stoppers for the DTaP-IPV and ActHIB vaccine components of Pentacel are not made with natural rubber latex.

Distributed by: Sanofi Pasteur Inc.
Manufactured by: Sanofi Pasteur Limited
Distributed by: Sanofi Pasteur Inc.
Switzerland USA

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Rx Only


16.2 Storage and Handling

Pentacel should be stored at 2°C to 8°C (35°F to 46°F). Do not freeze. Product which has been exposed to freezing should not be used. Do not use after expiration date shown on the label.

Pentacel should be used immediately after reconstitution.

17 PATIENT COUNSELING INFORMATION

Before administration of Pentacel, health-care personnel should inform the parent or guardian of the benefits and risks of the vaccine and the importance of completing the immunization series unless a contraindication to further immunization exists.

The health-care provider should inform the parent or guardian about the potential for adverse reactions that have been temporally associated with Pentacel or other vaccines containing similar ingredients.

The health-care provider should provide the Vaccine Information Statements (VIS) which are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization. The parent or guardian should be instructed to report adverse reactions to their health-care provider.

Manufactured by:
Sanofi Pasteur Limited
Toronto Ontario Canada

and
Sanofi Pasteur SA
Mancy L’Etoile France

Distributed by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

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