HIGHLIGHTS OF PRESCRIBING INFORMATION

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

Pentacel® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine Suspension for Intramuscular Injection

Initial U.S. Approval: 2008

RECENT MAJOR CHANGES

Dosage and Administration (2.1) 7/2022
Warnings and Precautions (5.8) 7/2022

INDICATIONS AND USAGE

• Pentacel is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis, polioviruses and invasive disease due to Haemophilus 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)

DOSE AND ADMINISTRATION

• 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 (DT aP-IPV component) and a lyophilized vaccine component (ActHIB vaccine). Reconstitute the ActHIB vaccine component with the DTaP-IPV component immediately before administration. (2.2)

DOSE FORMS AND STRENGTHS

• 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)

CONTRAINDICATIONS

• 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)

WARNINGS AND PRECAUTIONS

• Carefully consider benefits and risks before administering Pentacel to persons with a history of:
  - fever ≥40.5°C (≥104°F), hypotonic-hyporesponsive episode (HHE) or persistent, inconsolable 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)
  - 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. (5.3)
  - For infants and children with a history of previous seizures, an antipyretic may be administered (in the dosing recommended in its prescribing information) at the time of vaccination with Pentacel and for the next 24 hours. (5.4)
  - 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. (5.7)

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 inconsolable crying. Fever ≥38.0°C occurred in 6-16% 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)

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.

DRUG INTERACTIONS

• 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.

Revised: 10/2022

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Pentacel® is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis, poliomyelitis and invasive disease due to Haemophilus influenzae type b. Pentacel is approved for use as a four dose series in children 6 weeks through 4 years of age (prior to fifth birthday).

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Immunization Series

Pentacel is to be administered as a 4-dose series at 2, 4, 6 and 15-18 months of age. The first dose may be given as early as 6 weeks of age. Four doses of Pentacel constitute a primary immunization course against pertussis. Three doses of Pentacel constitute a primary immunization course against diphtheria, tetanus, H. influenzae type b invasive disease, and poliomyelitis; the fourth dose is a booster for diphtheria, tetanus, H. influenzae type b invasive disease, and poliomyelitis immunizations [see Clinical Studies (14.1, 14.2, 14.3, 14.4, 14.5)].

Mixed Sequences of Pentacel and other DTaP-containing Vaccines

Pentacel, DAPTACEL (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed), Quadracel (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine), and VAXELIS (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) contain the same pertussis antigens manufactured by the same process. The amount of each of the pertussis antigens is the same in Pentacel, Quadracel, and VAXELIS. Pentacel contains twice the amount of detoxified pertussis toxin (PT) and four times the amount of filamentous hemagglutinin (FHA) as DAPTACEL.
Pentacel may be used as the fourth dose in the 5-dose DTap series in children who have received a 3-dose series of VAXELIS [see CLINICAL STUDIES (14)].

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.

Children who have completed a 4-dose series with Pentacel should receive a fifth dose of DTPa vaccine using DAPTACEL or Quadracel at 4-6 years of age. (1) (2) 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. (3) 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. (3)

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 (Vial 1 of 2) component and a vial of lyophilized ActHIB (Vial 2 of 2) vaccine component. Before use, thoroughly but gently shake the vial of DTaP-IPV component, withdraw the entire liquid content and inject into the vial of the lyophilized ActHIB vaccine component. Gently swirl the vial now containing Pentacel until a cloudy, uniform, white to off-white (yellow tinge) suspension results. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Whenever solution and container permit. If these conditions exist, Pentacel should not be administered. Withdraw and administer a single 0.5 mL dose of Pentacel intramuscularly. 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 in 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 (1:100) 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 ≥30.5°C (≥85°F) within 48 hours, not attributable to another identifiable cause.

• Collapse or shock-like state (hypotonic-hyporesponsive episode [HHHE]) within 48 hours.

• Persistent, inconsolable 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. (4) 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 antipyretic 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

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.

5.8 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines including Pentacel. Procedures should be in place to avoid injury from fainting.

6 ADVERSE REACTIONS

Rates of adverse reactions varied by dose number. The most frequent (>50% of participants) systemic reactions following any dose were fussiness/irritability and inconsolable crying. The most frequent (>30% of participants) injection site reactions following any dose were tenderness and increased circumference of the injected arm.

6.1 Clinical Trials Experience

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 these events.

The poliovirus component (poliovirus types 1, 2, and 3) of this formulation of Pentacel is grown in Vero cells [see Description (11)]. The clinical study data in this section were accrued with a Pentacel formulation in which the poliovirus component was grown in MRC-5 cells. 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, 50.8% of participants were female. Among participants in the three US studies, 64.5% were Caucasian, 9.2% were Black, 12.9% 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>DAPTACEL + POLIOVAX + ActHIB</td>
<td>HCPDT + POLIOVAX + ActHIB at 2, 4, 6, and 15 months</td>
<td></td>
</tr>
<tr>
<td>50% of participants</td>
<td>Pentacel Control Vaccines Concomitantly Administered Vaccines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Number</td>
<td>Pentacel</td>
<td>Control Vaccines</td>
<td>Concomitantly Administered Vaccines</td>
</tr>
<tr>
<td>P3T06</td>
<td>DAPTACEL + IPOL + ActHIB at 2, 4, and 16 months</td>
<td>DAPTACEL + ActHIB at 15-16 months</td>
<td></td>
</tr>
<tr>
<td>50% of participants</td>
<td>Pentacel Control Vaccines Concomitantly Administered Vaccines</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7-valent pneumococcal conjugate vaccine (PCV7) at 2 and 6 months

Hepatitis B vaccine at 2 and 6 months

Hepatitis B vaccine at 2 and 6 months
### 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. Hepatitis B vaccine at 2 and 6 months (if a dose was previously administered) or at 2, 4, and 6 months (if no previous dose). 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>
</tbody>
</table>

### 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>Pentacel Dose 1 N=465-467%</th>
<th>Pentacel Dose 2 N=451%</th>
<th>Pentacel Dose 3 N=438-440</th>
<th>Pentacel Dose 4 N=367-396%</th>
<th>DAPTACEL + IPOL + ActHIB Dose 1 N=1,400-1,404</th>
<th>DAPTACEL + IPOL + ActHIB Dose 2 N=1,358-1,359</th>
<th>DAPTACEL + IPOL + ActHIB Dose 3 N=1,311-1,312</th>
<th>DAPTACEL + IPOL + ActHIB Dose 4 N=376-380</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redness &gt;5 mm</td>
<td>7.1</td>
<td>8.4</td>
<td>8.7</td>
<td>17.3</td>
<td>6.2</td>
<td>7.1</td>
<td>9.6</td>
<td>16.4</td>
</tr>
<tr>
<td>Redness &gt;25 mm</td>
<td>2.8</td>
<td>1.8</td>
<td>1.8</td>
<td>9.2</td>
<td>1.0</td>
<td>0.6</td>
<td>1.9</td>
<td>7.9</td>
</tr>
<tr>
<td>Redness &gt;50 mm</td>
<td>0.6</td>
<td>0.2</td>
<td>0.0</td>
<td>2.3</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Swelling &gt;5 mm</td>
<td>7.5</td>
<td>7.3</td>
<td>5.0</td>
<td>9.7</td>
<td>4.0</td>
<td>4.0</td>
<td>6.5</td>
<td>10.3</td>
</tr>
<tr>
<td>Swelling &gt;25 mm</td>
<td>3.0</td>
<td>2.0</td>
<td>1.6</td>
<td>3.8</td>
<td>1.6</td>
<td>0.7</td>
<td>1.1</td>
<td>4.0</td>
</tr>
<tr>
<td>Swelling &gt;50 mm</td>
<td>0.9</td>
<td>0.0</td>
<td>0.0</td>
<td>0.8</td>
<td>0.4</td>
<td>0.1</td>
<td>0.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Tenderness Moderate or Severe</td>
<td>47.5</td>
<td>39.2</td>
<td>42.7</td>
<td>56.1</td>
<td>48.8</td>
<td>38.2</td>
<td>40.9</td>
<td>51.1</td>
</tr>
<tr>
<td>Tenderness Severe</td>
<td>5.4</td>
<td>1.6</td>
<td>1.4</td>
<td>3.3</td>
<td>4.1</td>
<td>2.3</td>
<td>1.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Increase in Arm Circumference &gt;5 mm</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>33.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>30.6</td>
</tr>
<tr>
<td>Increase in Arm Circumference &gt;20 mm</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6.9</td>
</tr>
<tr>
<td>Increase in Arm Circumference &gt;40 mm</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.8</td>
</tr>
</tbody>
</table>

### Table 3: Systemic Reactions

<table>
<thead>
<tr>
<th>Systemic Reactions</th>
<th>Pentacel Dose 1 N=466-467%</th>
<th>Pentacel Dose 2 N=451-452%</th>
<th>Pentacel Dose 3 N=435-440</th>
<th>Pentacel Dose 4 N=369-398%</th>
<th>DAPTACEL + IPOL + ActHIB Dose 1 N=1,390-1,406</th>
<th>DAPTACEL + IPOL + ActHIB Dose 2 N=1,346-1,359</th>
<th>DAPTACEL + IPOL + ActHIB Dose 3 N=1,301-1,312</th>
<th>DAPTACEL + IPOL + ActHIB Dose 4 N=373-381</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever ≥38.0°C</td>
<td>5.8</td>
<td>10.9</td>
<td>16.3</td>
<td>13.4</td>
<td>9.3</td>
<td>16.1</td>
<td>15.8</td>
<td>8.7</td>
</tr>
<tr>
<td>Fever ≥38.5°C</td>
<td>1.3</td>
<td>2.4</td>
<td>4.4</td>
<td>5.1</td>
<td>1.6</td>
<td>4.3</td>
<td>5.1</td>
<td>3.2</td>
</tr>
<tr>
<td>Fever ≥39.0°C</td>
<td>0.4</td>
<td>0.0</td>
<td>0.7</td>
<td>0.3</td>
<td>0.1</td>
<td>0.4</td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Decreased Activity/Lethargy Moderate or Severe</td>
<td>45.6</td>
<td>32.7</td>
<td>32.5</td>
<td>24.1</td>
<td>51.1</td>
<td>37.4</td>
<td>33.2</td>
<td>24.1</td>
</tr>
<tr>
<td>Decreased Activity/Lethargy Severe</td>
<td>22.9</td>
<td>12.4</td>
<td>12.7</td>
<td>9.8</td>
<td>24.3</td>
<td>15.8</td>
<td>12.7</td>
<td>9.2</td>
</tr>
<tr>
<td>Decreased Activity/Lethargy Any</td>
<td>2.1</td>
<td>0.7</td>
<td>0.2</td>
<td>2.5</td>
<td>1.2</td>
<td>1.4</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Inconsolable Crying Any</td>
<td>59.3</td>
<td>49.8</td>
<td>47.3</td>
<td>35.9</td>
<td>58.5</td>
<td>51.4</td>
<td>47.9</td>
<td>36.2</td>
</tr>
<tr>
<td>Inconsolable Crying ≥1 hour</td>
<td>19.7</td>
<td>10.6</td>
<td>13.6</td>
<td>11.8</td>
<td>16.4</td>
<td>16.0</td>
<td>12.2</td>
<td>10.5</td>
</tr>
<tr>
<td>Inconsolable Crying &gt;3 hours</td>
<td>1.9</td>
<td>0.9</td>
<td>1.1</td>
<td>2.3</td>
<td>2.2</td>
<td>3.4</td>
<td>1.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Fussiness/Irritability Any</td>
<td>76.9</td>
<td>71.2</td>
<td>68.0</td>
<td>53.5</td>
<td>75.8</td>
<td>70.7</td>
<td>67.1</td>
<td>53.8</td>
</tr>
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</table>
Seizures

The frequency of reporting, or strength of evidence for a causal relationship to Pentacel, has not been reliably estimated from post-marketing surveillance data. Between 1997 and 2007, Pentacel was primarily used in children 6 weeks through 18 months of age and in children 5 to 16 years of age. The safety and effectiveness of Pentacel was established in the age group 6 weeks through 18 months of age and in children 5 to 16 years of age have not been established. The safety and effectiveness of Pentacel in the age group 19 months through 4 years is supported by evidence from studies in children 19 months through 4 years of age. The safety and effectiveness of Pentacel in children 5 to 16 years of age has not been established.

Across Studies 494-01, 494-03, 5A9908 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 Dose 1-3; N = 739 for Dose 4), or separately administered DAPTACEL + POLIO + ActHIB (1 participant; N = 1,455 for all at least one of Doses 1-3), or separately administered 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 in Study 494-01 had a possible seizure the same day as the third dose, and two participants in Study 5A9908 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 + POLIO + 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.

Seizure Symptoms

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 children 6 weeks through 18 months of age and in children 5 to 16 years of age. 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 infusion, inflammation, pain, abscesses and sterile abscesses, extensive swelling of the injected limb (including swelling that involved adjacent joints), vaccination failure/therapeutic response decreased (invasive H. influenzae type b disease)
- **Immune system disorders**
  - Anaphylaxis/anaphylactic reaction, hypersensitivity (such as rash and urticaria)
- **Infections and infestations**
  - Meningitis, rhinitis, viral infection
- **Metabolism and nutrition disorders**
  - Decreased appetite
- **Neurological disorders**
  - Somnolence, HHE, depressed level of consciousness
- **Psychiatric disorders**
  - Screaming
- **Respiratory, thoracic and mediastinal disorders**
  - Apnea, cough
- **Skin and subcutaneous tissue disorders**
  - Erythema, skin discoloration
- **Vascular disorders**
  - Pallor

### 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 (6) 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, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to Pentacel [see Warnings and Precautions (5.6)].

### 7.3 Drug/Laboratory Test Interactions

Antigenaemia 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.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.4 Pediatric Use

The safety and effectiveness of Pentacel was established in the age group 6 weeks through 18 months on the basis of clinical studies [see Clinical Trials Experience (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 children 6 weeks through 18 months. The safety and effectiveness of Pentacel in infants less than 6 weeks of age and in children 5 to 16 years of age have not been established.

### 11 DESCRIPTION

Pentacel consists of a Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus (DTP-aP-IPV) component and an ActHIB component combined through recombinant for uses in children as a single injection. ActHIB [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)], consists of H. influenzae type b capsular polysaccharide (polybetyl-rhotol-phosphate [PPP]) covalently bound to tetanus toxoid (TPP-T). The DTP-aP-IPV component is supplied as a sterile liquid used to reconstitute the lyophilized ActHIB component to form Pentacel. Pentacel is a uniform, cloudy, white-off-white (yellow tinge) suspension.

Each 0.5 mL dose contains 15 U diphtheria toxoid, 5 U tetanus toxoid, acellular pertussis antigens (20 mcg detoxified pertussis toxin (PT), 20 mcg filamentosus hemagglutinin (FHA), 3 mcg pertactin (PRN), 5 mcg fimbriae types 2 and 3 (FIM), inactivated polioviruses [29 D-antigen units (DU) Type 1 (Mahoney), 7 DU Type 2 (MEF-1), 26 DU Type 3 (Saukett)] and 10 mcg PRP of H. influenza type b covalently bound to 24 mg of tetanus toxoid (TPP-T).

Other ingredients per 0.5 mL dose include 1.5 mg aluminum phosphate (0.33 mg aluminum) as the adjuvant, <8.1 mcg polyarbortate 80, 3.3 mg (0.6% v/v) 2-phenoxethanol (not as a preservative), 42.5 mg sucrose, 2 mcg to 7 mcg residual formaldehyde, ≤50 ng residual glutaraldehyde, ≤10 ng residual bovine serum albumin, ≤0.001 mg streptomycin sulphate, ≤0.01 mg of neomycin and <0.000001 pg polymyxin B sulphate. Crotanobacter diethylphosphate is a modified Mueller’s growth medium. (7) After purification by ammonium sulfate fractionation, the diaphorin toxin is detoxified with formaldehyde and dialysis. Clostridium tetani is grown in modified Mueller’s growth medium without beef heart infusion. (8) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulfate fractionation and dialization. Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate. The acellular pertussis vaccine antigens are produced from Bordetella pertussis culture grown in Sigma-type medium (9) modified by the addition of casamino acids and dimethyl-beta-cysteine. 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, ultraltrification and chromatography. PT is detoxified with glutaraldehyde. FTA is treated with formaldehyde and the residual aldehydes are removed by ultratillation. The individual antigens are adsorbed separately onto aluminum phosphate.
The Type 1, Type 2, and Type 3 polioviruses are individually grown in Vero cells (a continuous line of monkey kidney cells). Prior to viral propagation, the cells are grown in isolation medium, supplemented with calf serum. For viral propagation, the culture medium is replaced by M199 medium without calf serum. The viral harvests are concentrated and purified, then inactivated with formaldehyde to produce monovalent suspensions of each serotype. Specified quantities of monovalent suspensions of each serotype are mixed to produce the trivalent poliovirus concentrate.

The adsorbed diphtheria, tetanus, and acellular pertussis antigens are combined with aluminum phosphate (as adjuvant), 2-phenoxethanol (not as a preservative) and water for injection, into an intermediate concentrate. The trivalent poliovirus concentrate is added and the DTaP-IPV component is diluted to its final concentration. The DTaP-IPV component does not contain a preservative.

Both diphtheria and tetanus toxoids induce at least 2 neutralizing units per mL in the guinea pig potency test. The potency of the acellular pertussis antigens is evaluated by the antibody response of immunized rabbits to detoxified PT, FHA, PRN and FIM as measured by enzyme-linked immunosorbent assay (ELISA). The potency of inactivated poliovirus antigens is determined by measuring antibody-mediated neutralization of poliovirus in sera from immunized rats.

PRP, a high molecular weight polymer, is prepared from the Haemophilus influenzae type b strain 1482 grown in a semi-synthetic medium. (10) The tetanus toxoid for conjugation to PRP is prepared by ammonium sulfate precipitation and formalin inactivation of the toxin from cultures of Clostridium tetani (Harvard strain) grown in a modified Mueller and Miller medium. (11) The toxoid is filter sterilized prior to the conjugation process. The ActHIB component does not contain a preservative. Potency of the ActHIB component is specified on each lot by limits on the content of PRP polysaccharide and protein per dose and the proportion of polysaccharide and protein that is characterized as high molecular weight conjugate.

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

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 are generally regarded as protective. (12) Levels of 1.0 IU/mL have been associated with long-term protection. (13)

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, measured by neutralization assay is considered the minimum protective level. (13) 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.

Polymyxin

Polymyxins, of which there are three serotypes (Types 1, 2, and 3) are enterotoxins. The presence of poliovirus type-specific neutralizing antibodies has been correlated with protection against poliovirus. (15)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Pentacel has not been shown to be 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. The poliovirus component (poliovirus types 1, 2 and 3) of this formulation of Pentacel is grown in Vero cells. (16) The polio- virus component of the two Pentacel formulations are analytically comparable. Serological correlates of protection exist for diphtheria, tetanus, polymyxins, and invasive disease due to H. influenzae type b. (17) Based on data from passive antibody studies and an efficacy study with H. influenzae type b polysaccharide vaccine in Finland, (17) 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 predicts protection through a subsequent one-year period. (18) These levels have been used to evaluate the effectiveness of Haemophilus b Conjugate Vaccines, including the ActHIB component of Pentacel.

Table 4: FHA, PRN and FIM Antibody Responses One Month Following Dose 3 of DAPTACEL in a Subset of Infants Vaccinated at 2, 4, 6, and 16 Months of Age in Sweden 1994-01

<table>
<thead>
<tr>
<th>FHA</th>
<th>PRN</th>
<th>FIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>% achieving 4-fold rise</td>
<td>GMC (EU/mL)</td>
<td>N = 407-454</td>
</tr>
<tr>
<td>68</td>
<td>80</td>
<td>97.9</td>
</tr>
<tr>
<td>60.70</td>
<td>71.46</td>
<td>91.75</td>
</tr>
<tr>
<td>129.85</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
of Pentacel against pertussis is unknown. Dose 4 of Pentacel relative to Dose 4 of DAPTACEL in US children correlates with diminished efficacy of 90% CI for ratio of GMCs (DAPTACEL/Pentacel) = 2.25]. Whether the lower anti-PRN GMC following DAPTACEL, non-inferiority criteria were met for all comparisons except for anti-PRN GMCs [upper limit of 90% CI for GMC ratio (DAPTACEL/Pentacel) <1.5 and upper limit of 90% CI for differences in rates (DAPTACEL minus Pentacel) <10%]. § Percent achieving 4-fold rise or GMC Post-Dose 3 Pentacel vaccine not inferior to Post-Dose 3 DAPTACEL vaccine [upper limit of 95% CI for difference in rates (DAPTACEL minus Pentacel) <10%]. ¶ Non-inferiority criterion is not met for GMC Post-Dose 4 Pentacel vaccine relative to Post-Dose 4 DAPTACEL vaccine [upper limit of 90% CI for GMC ratio (DAPTACEL/Pentacel) <1.5 and upper limit of 90% CI for differences in rates (DAPTACEL minus Pentacel) <10%].

In a separate study, Study P3T06, US infants were randomized to receive either Pentacel or DAPTACEL + IPOL + ActHIB at 2, 4, and 6, and 15-16 months of age (Table 1). The pertussis immune responses (GMCs and seroconversion rates) one month following the third and fourth doses were compared between the two groups (Table 5). Seroconversion was defined as a 4-fold rise in antibody level. Non-inferiority criteria were not met for seroconversion rates and GMCs following Dose 3 of Pentacel relative to Dose 3 of DAPTACEL. Following Dose 4 of Pentacel relative to Dose 4 of DAPTACEL, non-inferiority criteria were met for all comparisons except for anti-PRN GMCs [upper limit of 90% CI for ratio of GMCs (DAPTACEL/Pentacel) = 2.25]. Whether the lower anti-PRN GMC of Pentacel relative to Dose 4 of DAPTACEL in US children correlates with diminished efficacy of Pentacel against pertussis is unknown.

### 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

<table>
<thead>
<tr>
<th>Post-Dose 3 Pentacel N = 365</th>
<th>Post-Dose 3 DAPTACEL + IPOL + ActHIB N = 360</th>
<th>Post-Dose 4 Pentacel N = 365</th>
<th>Post-Dose 4 DAPTACEL + IPOL + ActHIB N = 360</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-PRP % achieving 4-fold rise</td>
<td>96.0[1]</td>
<td>93.6[1]</td>
<td>100.29</td>
</tr>
<tr>
<td>Anti-PT GMC (EU/mL)</td>
<td>102.6[1]</td>
<td>61.88</td>
<td>107.89[1]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-Dose 3 Pentacel N = 218-318</th>
<th>Post-Dose 3 DAPTACEL + IPOL + ActHIB N = 714-1,016</th>
<th>Post-Dose 4 Pentacel N = 230-367</th>
<th>Post-Dose 4 DAPTACEL + IPOL + ActHIB N = 237-347</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-FHA % achieving 4-fold rise</td>
<td>81.9[1]</td>
<td>60.9</td>
<td>88.4[1]</td>
</tr>
<tr>
<td>Anti-FHA GMC (EU/mL)</td>
<td>73.68[1]</td>
<td>29.22</td>
<td>107.94[1]</td>
</tr>
<tr>
<td>Anti-PRN % achieving 4-fold rise</td>
<td>74.2[1]</td>
<td>75.4</td>
<td>92.7[1]</td>
</tr>
<tr>
<td>Anti-PRN GMC (EU/mL)</td>
<td>36.05[1]</td>
<td>43.25</td>
<td>93.5[1]</td>
</tr>
<tr>
<td>Anti-FIM % achieving 4-fold rise</td>
<td>91.7[1]</td>
<td>86.3</td>
<td>93.5[1]</td>
</tr>
</tbody>
</table>

- **Anti-FIM**
- **Anti-PRN**
- **Anti-PT**
- **Anti-FHA**

Study P3T06 was a study conducted in the US, where infants were randomized to receive 3 doses of VAXELIS at 2, 4, and 6 months of age and Pentacel at 15 months of age (N = 2,406), or control group vaccines (4 doses of Pentacel at 2, 4, 6, and 15 months of age = RECOMBIVAX HB [Hepatitis B Vaccine (Recombinant)] at 2 and 6 months of age; N = 402). All subjects received concomitant Pneumococcal 13 (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein]) at 2, 4, and 6, and 15 months of age.

Participants were evaluated for immune responses to pertussis antigens one month following the dose of Pentacel administered at 15 months of age. The non-inferiority criteria for antibody vaccine response rates and GMCs for all pertussis antigens were met following the fourth dose except for GMCs for PRN (lower bound of 2-sided 95% CI for GMC ratio [VAXELIS group/Control group vaccines] was 0.66, which was below the non-inferiority criterion of >0.67). (20)

### 14.4 Polymyelitis

In Study P3T06 (Table 1), in which infants were randomized to receive the first three doses of Pentacel or DAPTACEL + IPOL + ActHIB at 2, 4, and 6 months of age, one month following the third dose of study vaccines, >39.4% of participants in both groups (Pentacel: N = 338-350), (DAPTACEL + IPOL + ActHIB: N = 1,050-1,097) achieved neutralizing antibody levels of ≥1.8 for Polioviruses types 1, 2, and 3.

In Study 494-01 (Table 1), in which infants were randomized to receive Pentacel or HCPDT + POLIOVAX + ActHIB, GMFs (1/dil) of antibodies to Polioviruses types 1, 2, and 3 one month following Dose 4 of Pentacel (N = 851-857) were 2,304, 4,178, and 4,415, respectively, and one month following Dose 4 of POLIOVAX (N = 224-287) were 2,330, 2,840, and 3,300, respectively.

### 14.5 Invasive Disease due to H. Influenzae Type b

Anti-PRP seroprotection rates and GMCs one month following Dose 3 of Pentacel or separately administered ActHIB in studies 494-01, P3T06, and MSA10 are presented in Table 6. In Study 494-01, non-inferiority criteria were not met for the proportion of participants who achieved an anti-PRP level ≥1.0 mcg/mL and for anti-PRP GMCs following Pentacel compared with separately administered ActHIB. In each of Studies P3T06 and MSA10, the non-inferiority criterion was met for the proportion of participants who achieved an anti-PRP level ≥1.0 mcg/mL following Pentacel compared with separately administered ActHIB. In Study MSA10, the non-inferiority criterion was met for anti-PRP GMCs following Pentacel compared with separately administered ActHIB.

### 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

<table>
<thead>
<tr>
<th>Study 494-01 DAPTACEL + IPOL + ActHIB N = 401</th>
<th>Study P3T06 DAPTACEL + IPOL + ActHIB N = 365</th>
<th>Study P3T06 Pentacel N = 1,128</th>
<th>Study 494-01 HCPDT + POLIOVAX + ActHIB N = 401</th>
</tr>
</thead>
<tbody>
<tr>
<td>% achieving anti-PRP ≥0.15 mcg/mL</td>
<td>95.4[1]</td>
<td>98.3</td>
<td></td>
</tr>
<tr>
<td>% achieving anti-PRP ≥1.0 mcg/mL</td>
<td>79.1[1]</td>
<td>88.6</td>
<td></td>
</tr>
<tr>
<td>Anti-PRP GMC (mcg/mL)</td>
<td>3.19[1]</td>
<td>6.23</td>
<td></td>
</tr>
<tr>
<td>Study P3T06 Pentacel N = 365</td>
<td>Study P3T06 Pentacel N = 1,128</td>
<td>Study 494-01 HCPDT + POLIOVAX + ActHIB N = 401</td>
<td></td>
</tr>
<tr>
<td>% achieving anti-PRP ≥0.15 mcg/mL</td>
<td>92.3[1]</td>
<td>93.3</td>
<td></td>
</tr>
<tr>
<td>% achieving anti-PRP ≥1.0 mcg/mL</td>
<td>72.1[1]</td>
<td>70.8</td>
<td></td>
</tr>
<tr>
<td>Anti-PRP GMC (mcg/mL)</td>
<td>2.31[1]</td>
<td>2.29</td>
<td></td>
</tr>
</tbody>
</table>

- **Anti-PRP**
- **Anti-FIM**
- **Anti-PRN**
- **Anti-PT**
- **Anti-FHA**
- **Anti-FIM**

Data on anti-PT levels using an adequately specific assay were not available. Data on anti-PT levels using an adequately specific assay were not available.
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 M5A10 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>MSA10 Pentacel N = 826</th>
<th>Study MSA10 DAPTACEL + 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>73.1‡</td>
<td>74.8</td>
</tr>
<tr>
<td>Anti-PRP GMC (mcg/mL)</td>
<td>2.52*</td>
<td>2.38</td>
</tr>
</tbody>
</table>

Per Protocol Immunogenicity population for all studies. IPV indicates Poliovirus Vaccine Inactivated.

† 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 limit of 90% CI for difference in rates (ActHIB minus Pentacel) ≥1.0 mcg/mL].
§ Non-inferiority criterion not met for GMC following Pentacel vaccine relative to ActHIB vaccine [upper limit of 90% CI of GMC ratio (ActHIB/Pentacel), 2.26, exceeds the non-inferiority criterion <1.5].
¶ Non-inferiority criterion not pre-specified.
# GMC following Pentacel vaccine not inferior to ActHIB vaccine [upper limit of 95% 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, 66.8% of Pentacel recipients (N = 829) and 80.6% of separately administered ActHIB recipients (N = 276) had an anti-PRP level ≥0.15 mcg/mL. Following Dose 4 of study vaccines, 92.6% of Pentacel recipients (N = 874) and 96.4% of separately administered ActHIB recipients (N = 291) 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, 97.3% 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-HBsAg ≥10 mIU/mL and GMCs) or PCV7 (percent of participants with antibody levels ≥0.5 mcg/mL, and GMCs to each serotype) administered concomitantly with Pentacel (N = 321-325) relative to these vaccines administered concomitantly with DAPTACEL + IPOL + ActHIB (N = 998-1,029). The immune responses to hepatitis B vaccine and PCV7 were evaluated one month following the third dose.

In Study 494-01, (Table 1) there was no evidence for interference in the immune response to the fourth dose of PCV7 (percent of participants with antibody levels ≥0.5 mcg/mL and ≥0.5 mcg/mL and GMCs to each serotype) administered concomitantly with MMR and varicella vaccines (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 seroresponsiveness 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 DAPTACEL® [full prescribing information]. Toronto, ON: Sanofi Pasteur Limited.
2 Quadracel® [full prescribing information]. Toronto, ON: Sanofi Pasteur Limited.
12 Department of Health and Human Services, Food and Drug Administration. Biological products; bacterial vaccines and toxoids; implementation of efficacy review; proposed rule. Federal Register 1985;50(240):5102-17.
20 VAXELIS® [full prescribing information]. Distributed by: Sanofi Pasteur Inc. Swiftwater PA 18370 USA

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.

5 Dose Package (NDC No. 49281-511-05) containing 5 vials of DTAp-IPV (Vial 1 of 2 component (NDC No. 49281-561-01) to be used to reconstitute 5 single-dose vials of lyophilized ActHIB (Vial 2 of 2) vaccine component (NDC No. 49281-544-58).

16.2 Storage and Handling

Pentacel should be stored at 2° to 8°C (35° 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.

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
Marcy L’Etoile France

Distributed by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

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R2-1022 USA

DTPPV-FLR-SL-OCTT2 Rx Only