INDICATIONS AND USAGE

Adacel® (Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed), Suspension for Intramuscular Injection

Initial U.S. Approval: 2005

- Adacel is a vaccine indicated for active booster immunization against tetanus, diphtheria and pertussis. Adacel is approved for use in persons 10 through 64 years of age. (1)

DOSE AND ADMINISTRATION

For intramuscular injection only.
- Each dose of Adacel is administered as a 0.5 mL injection. (2.1)
- For routine booster vaccination, a first dose of Adacel is administered 5 years or more after the last dose of Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) series or 5 years or more after vaccination with Tetanus and Diphtheria Toxoids Adsorbed (Td). A second dose of Adacel may be administered 8 years or more after the first dose with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap).
- Adacel may be administered for tetanus prophylaxis for wound management. For management of a tetanus prone wound, a booster dose of Adacel may be administered if at least 5 years have elapsed since previous receipt of a tetanus toxoid containing vaccine. (2.2)

DOSE FORMS AND STRENGTHS

- Single-dose vials and prefilled syringes containing a 0.5 mL suspension for injection. (3)

CONTRAINDICATIONS

- Severe allergic reaction (eg, anaphylaxis) to any component of Adacel or any other diphtheria toxoid, tetanus toxoid and pertussis antigen-containing vaccine. (4.1)
- Encephalopathy (eg, coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous pertussis antigen-containing vaccine. (4.2)

WARNINGS AND PRECAUTIONS

- The tip caps of the prefilled syringes may contain natural rubber latex, which may cause allergic reactions in latex sensitive individuals. (5.2, 17)
- 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 a subsequent dose of Adacel vaccine. (5.3)

ADVERSE REACTIONS

- Following the first vaccination with Adacel, the most common solicited reactions occurring within 0–14 days of vaccination for Adolescents (11–17 years of age)/Adults (18–64 years of age) were: injection site pain (77.8%/85.6%), headache (43.7%/33.5%), body ache or muscle weakness (30.4%/21.9%), tiredness (30.2%/24.3%), injection site swelling (20.9%/21.0%), and injection site erythema (20.6%/24.7%). (6.1)

DRUG INTERACTIONS

- When Adacel was administered concomitantly with trivalent inactivated influenza vaccine (TIV) to adults 19–64 years of age, a lower antibody response was observed for pertussis antigen as compared to Adacel administered alone. (7.1, 14.4)
- Immunosuppressive therapies may reduce the immune response to Adacel. (7.2)
- Do not mix Adacel with any other vaccine in the same syringe or vial.

USE IN SPECIFIC POPULATIONS

- Pregnancy Exposure Registry: contact Sanofi Pasteur Inc. at 1-800-822-2463 (1-800-VAC-CINE) or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

PATIENT COUNSELING INFORMATION

Revise:

01/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
9 USE IN SPECIFIC POPULATIONS
10 DESCRIPTION
11 CLINICAL PHARMACOLOGY
12 NONCLINICAL TOXICOLOGY
13 CLINICAL STUDIES
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
3 DOSE FORMS AND STRENGTHS

Adacel is a suspension for injection available in 0.5 mL single-dose vials and prefilled syringes. [See HOW SUPPLIED/STORAGE AND HANDLING (16)].

4 CONTRAINDICATIONS

4.1 Hypersensitivity

A severe allergic reaction (eg, anaphylaxis) after a previous dose of any tetanus toxoid, diphtheria toxoid or pertussis containing vaccine or any other component of this vaccine is a contraindication to administration of Adacel. [See DESCRIPTION (11)]. Because of uncertainty as to which component of the vaccine may be responsible, none of the components should be administered. Alternatively, such individuals may be referred to an allergist for evaluation if further immunizations are to be considered.

4.2 Encephalopathy

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

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 Latex

For one presentation of Adacel, the tip caps of the prefilled syringes may contain natural rubber latex, which may cause allergic reactions in latex sensitive individuals. The vial stopper is not made with natural rubber latex. [See HOW SUPPLIED/STORAGE AND HANDLING (16)].

5.3 Guillain-Barré Syndrome and Brachial Neuritis

A review by the Institute of Medicine found evidence for acceptance of a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome. (1) If Guillain-Barré syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the risk for Guillain-Barré syndrome may be increased following a dose of Adacel.

5.4 Progressive or Unstable Neurologic Disorders

Progressive or unstable neurologic conditions are reasons to defer Adacel. It is not known whether administration of Adacel to persons with an unstable or progressive neurologic disorder might hasten manifestations of the disorder or affect the prognosis. Administration of Adacel to persons with an unstable or progressive neurologic disorder may result in diagnostic confusion between manifestations of the underlying illness and possible adverse effects of vaccination.

5.5 Arthur’s-Patient Hypersensitivity

Persons who experienced an Arthur’s-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine should not receive Adacel unless at least 10 years have elapsed since the last dose of a tetanus toxoid containing vaccine.

5.6 Altered Immune Competence

If Adacel 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 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccine, including Adacel. Procedures should be in place to prevent falling injury and manage syncope reactions.

6 ADVERSE REACTIONS

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 those events. As with any vaccine, there is the possibility that broad use of Adacel could reveal adverse reactions not observed in clinical trials.

The safety of a first vaccination with Adacel was evaluated in 5 clinical studies. Three of the studies were conducted in the U.S. and 2 were conducted in Canada. Of the study participants, 86% were Caucasian, 8% Black, 3% Hispanic, 1% Asian and 2% of other ethnic origin. A total of 7,143 individuals 10 through 64 years of age inclusive (4,895 adolescents 10 through 17 years of age and 2,248 adults 18 through 64 years of age) received a single dose of Adacel.

U.S. Adolescent and Adult Study of a First Vaccination with Adacel (TD506)

Clinical study TD506 was a randomized, observer-blind, active-controlled trial that enrolled adolescents 11 through 17 years of age (Adacel N = 1,184; DECAVAC (Tetanus and Diphtheria Toxoids Adsorbed; manufactured by Sanofi Pasteur Inc., Swiftwater, PA) N = 782) and adults 18 through 64 years of age (Adacel N = 1,752; DECAVAC N = 573). Study participants had not received tetanus or diphtheria containing vaccines within the previous 5 years. Solicited local and systemic reactions and unsolicited adverse events were monitored daily for 14 days post vaccination using a diary card. From days 14 to 28 post vaccination, information on adverse events necessitating a medical contact, such as a telephone call, visit to an emergency room, physician’s office or hospitalization, was obtained via telephone interview or at an interim clinic visit. From days 28 to 6 months post vaccination, participants were monitored for unexpected visits to a physician’s office or to an emergency room, onset of serious illness, and hospitalizations. Information regarding adverse events that occurred in the 6-month post-vaccination time period was obtained from participants via telephone contact. At least 98% of participants completed the 6-month follow-up evaluation.

The frequency of selected solicited adverse reactions (erythema, swelling, pain and fever) occurring during days 0 to 14 following vaccination with Adacel or Td vaccine in adolescents 11 through 17 years of age and adults 18 through 64 years of age are presented in Table 1. Most of these reactions were reported at a similar frequency in recipients of both Adacel and Td vaccine. Pain at the injection site was the most common adverse reaction in 62.9% to 77.8% of all vaccinees. In addition, overall rates of pain were higher in adolescent recipients of Adacel compared to Td vaccine recipients. Rates of moderate and severe pain in adolescents did not significantly differ between the Adacel and Td vaccine groups. Among adults, the rates of pain after receipt of Adacel or Td vaccine did not significantly differ. Fever of 38°C and higher was uncommon, although in the adolescent age group it occurred significantly more frequently in Adacel recipients than Td vaccine recipients.

Table 1: Frequencies of Solicited Injection Site Reactions and Fever for Adolescents and Adults, Days 0-14, Following a First Vaccination with Adacel or Td Vaccine in Study TD506

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Adolescents 11-17 years</th>
<th>Adults 18-64 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adacel N</td>
<td>1,174-1,175 (%)</td>
<td>1,697-1,698 (%)</td>
</tr>
<tr>
<td>Td N</td>
<td>782-787 (%)</td>
<td>573-573 (%)</td>
</tr>
<tr>
<td>Fever</td>
<td>≥38.0°C (≥100.4°F)</td>
<td>≥38.8°C to ≥39.4°C (≥100.0°F to ≥103.0°F)</td>
</tr>
<tr>
<td></td>
<td>0.2 (0.0)</td>
<td>0.6 (0.0)</td>
</tr>
</tbody>
</table>

The study sample size was designed to detect >10% differences between Adacel and Td vaccines for events of ‘Any’ intensity.

†N = number of participants with available data.

‡Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Inc., Swiftwater, PA.

§Adacel did not meet the non-inferiority criterion for rates of ‘Any’ Pain in adolescents compared to Td vaccine rates (upper limit of the 95% CI on the difference for Adacel minus Td vaccine was 10.7% whereas the criterion was <10%).

¶Interfered with activities, but did not necessitate medical care or absenteeism.

¶¶Incapacitating, prevented the performance of usual activities, may have/or did necessitate medical care or absenteeism.

The frequency of other solicited adverse reactions (days 0-14) are presented in Table 2. The rates of these reactions following a first vaccination with Adacel were comparable with those observed with Td vaccine. Headache was the most frequent systemic reaction and was usually of mild to moderate intensity.

Table 2: Frequencies of Other Solicited Adverse Reactions for Adolescents and Adults, Days 0-14, Following a First Vaccination with Adacel or Td Vaccine in Study TD506

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Adolescents 11-17 years</th>
<th>Adults 18-64 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adacel N</td>
<td>1,174-1,175 (%)</td>
<td>1,697-1,698 (%)</td>
</tr>
<tr>
<td>Td N</td>
<td>782-787 (%)</td>
<td>573-573 (%)</td>
</tr>
<tr>
<td>Headache</td>
<td>Any</td>
<td>33.9 (34.1)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>11.4 (10.5)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>2.8 (2.1)</td>
</tr>
<tr>
<td>Body Ache or Muscle Weakness</td>
<td>Any</td>
<td>21.9 (18.8)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>6.1 (5.7)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>1.2 (0.9)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>Any</td>
<td>6.9 (6.1)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>7.5 (8.5)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>1.0 (1.3)</td>
</tr>
</tbody>
</table>

The frequency of other solicited adverse reactions (days 0-14) are presented in Table 2. The rates of these reactions following a first vaccination with Adacel were comparable with those observed with Td vaccine. Headache was the most frequent systemic reaction and was usually of mild to moderate intensity.
Injection site and systemic solicited reactions occurred at similar rates in Adacel and Td vaccine recipients in the 3 day post-vaccination period. Most injection site reactions occurred within the first 3 days after vaccination (with a mean duration of less than 3 days). The rates of unsolicited adverse events reported from days 14-28 post-vaccination were comparable between the two vaccine groups, as were the rates of unsolicited adverse events from day 28 through 6 months. There were no spontaneous reports of extensive limb swelling of the injected limb in study Td506, nor in the other three studies which also contributed to the safety database for Adacel.

In a randomized, observer-blind, active-controlled, multicenter study (Td537), adults 18 through 64 years of age who had received a first dose of Adacel 8-12 years previously were enrolled and randomized to receive either Adacel (N = 1002) or a US licensed Td vaccine, TENIVAC (Tetanus and Diphtheria Toxoids Adsorbed; manufactured by Sanofi Pasteur, Limited) (N = 328). Subjects were recruited from the primary licensure study Td506 and the Canadian general public and had not received Diphtheria and Tetanus toxoid, reduced diphtheria toxoid (Td) vaccine within 28 days of the experimental visit or via telephone interview for the duration of the trial, ie, up to 6 months post-vaccination.

In the concomitant vaccination study with Adacel (first vaccination) and Hepatitis B vaccine [Recombivax HB] (Td501) [See CLINICAL STUDIES (14)], injection site and systemic adverse events were monitored daily for 14 days post-vaccination using a diary card. Injection site adverse events were only monitored at site/Arm of Adacel administration. Unsolicited reactions (including immediate reactions, serious adverse events and events that elicited seeking medical attention) were collected at a clinic visit or by telephone interview for the duration of the trial, ie, up to 6 months post-vaccination.

In the concomitant vaccination study with Adacel (first vaccination) and Influenza Vaccine (TIV) [Fluzone] (Td502) [See CLINICAL STUDIES (14)], injection site and systemic adverse events were monitored on days 1-7 post-vaccination using a diary card. All unsolicited reactions occurring through day 14 were collected. From day 14 to the end of the trial, ie, up to 6 months post-vaccination. The rates of fever and injection site erythema, swelling and/or joint complaints were reported by 22.5% for concomitant vaccination and 17.5% for separate administration at the Adacel administration site were increased when coadministered. Swollen and/or sore joints were reported by 22.5% for concomitant vaccination and 17.5% for separate administration at the Adacel administration site.

### Table 2: Frequencies of Other Solicited Adverse Reactions for Adolescents and Adults, Days 0-14, Following a First Vaccination with Adacel or Td Vaccine in Study Td506 (continued)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Adolescents 11-17 years</th>
<th>Adults 18-64 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adacel (N= 1,174-1,175)</td>
<td>Td506 (N= 787)</td>
</tr>
<tr>
<td></td>
<td>Td501 (N= 1,097-1,698)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Td502 (N= 560-561)</td>
<td></td>
</tr>
<tr>
<td>Chills</td>
<td>Any</td>
<td>15.1</td>
</tr>
<tr>
<td></td>
<td>Moderate§</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Severe§</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>11.3</td>
</tr>
<tr>
<td></td>
<td>Moderate§</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>Severe§</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>13.3</td>
</tr>
<tr>
<td></td>
<td>Moderate§</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Severe§</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>6.6</td>
</tr>
<tr>
<td></td>
<td>Moderate§</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Severe§</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>10.3</td>
</tr>
<tr>
<td></td>
<td>Moderate§</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Severe§</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>4.6</td>
</tr>
<tr>
<td></td>
<td>Moderate§</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>Severe§</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>2.7</td>
</tr>
</tbody>
</table>

### Table 3: Frequencies of Solicited Adverse Reactions 0-7 Days Following a Second Vaccination with Adacel Compared to Td Vaccine in Study Td537 - Safety Analysis Set (continued)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Adacel (N=999) (%)</th>
<th>Td Adsorbed (N=328) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site swelling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 (≤51 to ≤100 mm)</td>
<td>6.9</td>
<td>8.0</td>
</tr>
<tr>
<td>Grade 3 (&gt;100 mm)</td>
<td>2.4</td>
<td>2.2</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>0.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Malaise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>41.4</td>
<td>39.1</td>
</tr>
<tr>
<td>Grade 3</td>
<td>12.4</td>
<td>10.5</td>
</tr>
<tr>
<td>Myalgia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>33.3</td>
<td>30.8</td>
</tr>
<tr>
<td>Grade 3</td>
<td>3.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>

N = number of participants with available data.
§Significant; prevents daily activity
†Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur, Inc., Swiftwater, PA.
*If some of the reactions are severe, withdrawals and/or discontinuations were made.
¶Statistically higher rates following concurrent administration (66.6%) versus separate administration.
| Injection site erythema | Any | 87.1 |
| Grade 2 | 28.5 |
| Grade 3 | 3.6 |
| Injection site swelling | Any | 6.4 |
| Grade 2 (≤51 to ≤100 mm) | 2.1 |
| Grade 3 (>100 mm) | 0.2 |

In the concomitant vaccination study with Adacel (first vaccination) and Influenza Vaccine (TIV) [Fluzone] (Td502) [See CLINICAL STUDIES (14)], injection site and systemic adverse events were monitored on days 1-7 post-vaccination using a diary card. All unsolicited reactions occurring through day 14 were collected. From day 14 to the end of the trial, ie, up to 6 months post-vaccination. The incidence of other solicited and unsolicited adverse events was not different between the 2 study groups.
post-vaccination using a diary card. Unsolicited adverse events and serious adverse events were collected for 28 days after vaccination. Pain was the most frequently reported local event occurring in approximately 88% of all participants. Headache was the most frequently reported systemic event occurring in approximately 44% of all participants. Soreness/swollen/joint reactions were reported by approximately 14% of participants. Most joint complaints were mild in intensity with a mean duration of 2 days.

An additional 962 adolescents and adults received Adacel in three supportive Canadian studies (TC9704, TS9707 and TD9805) used as the basis for licensure in other countries. Within these clinical trials, the rates of local and systemic reactions following the first vaccination with Adacel were similar to those reported in the 18-month clinical trials in the U.S. with the exception of a higher rate (68%) of adults experiencing “any” local injection site pain. The rate of severe pain (0.8%), however, was comparable to the rates reported in four principal trials conducted in the US. There was one spontaneous report of whole-arm swelling of the injected limb among the 277 TD vaccine recipients, and two spontaneous reports among the 862 Adacel recipients in the supportive Canadian studies. An additional study (TD919) enrolled 3,102 individuals in an open label, two-arm, multicenter trial (65 participants in each group) to evaluate the safety and immunogenicity of a first vaccination with Adacel administered to persons 10 to <17 years of age compared to persons 11 to <12 years of age. Immediate reactions were collected before post-vaccination. Solicited local and systemic events were monitored for 7 days post-vaccination using a diary card. Unsolicited and serious adverse events were collected for approximately 30 days post-vaccination. Similar rates of immediate, solicited and unsolicited adverse reactions were reported in each of the two age cohorts. One serious adverse event, not related to vaccination, was reported in the younger age group.

Serious Adverse Events

Throughout the 6-month follow-up period following a first vaccination with Adacel in study TD919, SEAEs were reported in 1.5% of Adacel recipients and in 1.4% of TD vaccine recipients. Two SEAEs in adults were neurological events that occurred within 28 days of Adacel administration; one severe migraine with unilateral facial paralysis and one diagnosis of nerve compression in neck and left arm. Similar or lower rates of serious adverse events were reported in the other trials following a first vaccination with Adacel in participants up to 64 years of age and no additional neuropathic events were reported. In study TD919, follow-up of vaccination of Adacel was administered 6-12 years after the initial vaccination of Adacel, a total of 8 participants (0.8%) in the Adacel group and 1 participant (0.3%) in the TD group reported SEAEs during the 6-month follow-up period. All SEAEs were considered by the investigator to be unrelated to the study vaccine. In study TD918, seven participants experienced an SAE, all of which were considered by the investigator to be unrelated to the study vaccine.

5.2 Postmarketing Experience

The following adverse events have been spontaneously reported in the US and other countries. 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 Adacel.

• Immunologic system disorders

  • Anaphylactic reaction, hypersensitivity reaction (angioedema, edema, rash, hypotension)

• Nervous system disorders

  • Paresthesia, hypopnea, Guillain-Barré syndrome, brachial neuritis, facial palsy, convulsion, syncope, myelitis

• Cardiac disorders

  • Myocarditis

• Skin and subcutaneous tissue disorders

  • Pruritus

• Musculoskeletal and connective tissue disorders

  • Myositis, muscle spasm

• General disorders and administration site conditions

  • Injection site reactions (>50 mm), extensive limb swelling from the injection site beyond one or both joints

  • Injection site bruising, sterile abscesses, Arthus hypersensitivity

7 DRUG INTERACTIONS

7.1 Concomitant Vaccination

When Adacel is administered concomitantly with other injectable vaccines or Tetanus Immune Globulin, they should be given with separate syringes and at different injection sites. Adacel should not be mixed with any other vaccine in the same syringe or vial.

In a clinical study Adacel (first vaccination) was administered concomitantly with a US-licensed trivalent inactivated influenza vaccine (TIV). [See ADVERSE REACTIONS (6.1) and CLINICAL STUDIES (14).] No interference in tetanus and diphtheria seroprotection rates and responses to influenza vaccine, detoxified pertussis toxin (PT), fimbrae types 2 and 3 (FIM) or filamentous hemagglutinin (FHA) were observed when Adacel was administered concomitantly with TIV compared to separate administration. A lower pertactin (PRN) GMC was observed when Adacel was administered concomitantly with TIV compared to separate administration.

7.2 Immunosuppressive Treatments

Immunosuppressive therapies, including radiation, antimitabolics, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. [See WARNINGS AND PRECAUTIONS (5.6).]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

A pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Adacel during pregnancy. Women who receive Adacel during pregnancy are encouraged to contact directly, or have their healthcare professional contact, Sanofi-pasteur Inc. at 1-800-822-2463 (1-800-VACCINE).

Risk Summary

All pregnancies have a risk of birth defect, loss or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies of 1 in every 100 to 2%, respectively. There are no adequate and well-controlled studies of Adacel administration in pregnant women in the U.S. Available data suggest the rates of major birth defects and miscarriage in women who receive Adacel within 30 days prior to pregnancy or during pregnancy are consistent with estimated background rates. (See Data)
13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Adacel has not been evaluated for carcinogenic or mutagenic potential, or impairment of male fertility.

14 CLINICAL STUDIES

The effectiveness of the tetanus toxoid and diphtheria toxoid used in Adacel was based on the immune response to these antigens compared to a US licensed Td and Diphtheria and Tetanus Toxoids Adsorbed For Adult Use (Td) vaccine manufactured by Sanofi Pasteur Inc., Swiftwater, PA. The primary measures for immune response to the diphtheria and tetanus toxoids were the percentage of participants attaining an antibody level of at least 0.1 IU/mL.

The effectiveness of the pertussis antigens used in Adacel was evaluated based on a comparison of pertussis antibody levels achieved in recipients of Adacel with those obtained in infants after three or four doses of DAPTACEL. For the first dose of Adacel, the comparisons were to infants who received three doses of DAPTACEL in the Sweden I Efficacy Trial. For the second dose of Adacel, for the evaluation of FHA, PRN, and FIM antibody levels, the comparisons were to infants who received three doses of DAPTACEL in the Sweden I Efficacy trial; for evaluation of PT antibody levels, the comparison was to infants who received four doses of DAPTACEL in a US safety and immunogenicity study (Study MSA10). In the Sweden I Efficacy Trial, three doses of DAPTACEL vaccine were shown to confer a protective efficacy of 84.9% (95% CI: 80.1%, 88.6%) against WHO defined pertussis (21 days of paroxysmal cough with laboratory-confirmed B pertussis infection or epidemiological link to a confirmed case). The protective efficacy against mild pertussis (defined as at least one day of cough with laboratory-confirmed B pertussis infection) was 77.9% (95% CI: 72.6%, 82.2%).

In addition, the ability of Adacel to elicit a booster response (defined as rise in antibody concentration after vaccination) to the tetanus, diphtheria and pertussis antigens following vaccination was evaluated.

14.1 Immunological Evaluation in Adolescents and Adults, 11 through 64 Years of Age Following a First Vaccination with Adacel

Study Td506 was a comparative, multi-center, randomized, observer-blind, controlled trial which enrolled 4,480 participants; 2,053 adolescents (11-17 years of age) and 2,427 adults (18-64 years of age). Enrollment was stratified by age to ensure adequate representation across the entire age range. Participants had not received a tetanus or diphtheria toxoid containing vaccine within the previous 5 years. After enrollment participants were randomized to receive one dose of either Adacel or Td vaccine. A total of 4,461 randomized participants were vaccinated. The per-protocol immunogenicity subset included 1,270 Adacel recipients and 1,026 Td vaccine recipients. Sera were obtained before and approximately 35 days after vaccination. (Blinding procedures for safety assessments are described in ADVERSE REACTIONS (6).) Demographic characteristics were similar within age groups and between the vaccine groups. A total of 76% of the adolescents and 1.1% of the adults reported a history of receiving 5 previous doses of diphtheria-tetanus-pertussis containing vaccines. Anti-tetanus and anti-diphtheria seroprotection rates (≥0.1 IU/mL) and booster response rates were comparable between Adacel and Td vaccines.

Table 6: Ratio of Pertussis Antibody Geometric Mean Concentrations (GMCS) Observed One Month Following A First Vaccination with Adacel in Adolescents and Adults 11 through 64 Years of Age Compared With Those Observed in Infants One Month Following Vaccination at 2.4 and 6 Months of Age in the Efficacy Trial with DAPTACEL (Sweden I Efficacy Study)

Table 7: Booster Response Rates to the Pertussis Antigens Observed One Month Following A First Vaccination with Adacel in Adolescents and Adults 11 through 64 Years of Age
Study Td59 assessed the comparative immunogenicity of a first vaccination with Adacel administered to adolescents (10 to <11 years of age) in the 1st through 4th year of age in the 5th year. In this study non-inferiority was demonstrated for booster responses to tetanus and diphtheria toxoids. GMCs to the pertussis antigens PT, FHA, PRN and FIM and booster responses to the pertussis antigens PT, FHA and PRN. For FIM, non-inferiority was not demonstrated as the lower bound of the 95% CI of the difference in booster response rates (−5.98%) did not meet the predefined criterion (≤−5% when the booster response in the older age group was ≥95%).

14.2 Immunological Evaluation in Adults, 18 through 64 Years of Age Following a Second Vaccination with Adacel

In study Td506 (See ADVERSE REACTIONS (6.1)), subjects 18 to 64 years of age who had received a dose of Adacel 8-12 years previously, were randomized to receive a second dose of Adacel or Td vaccine (Tetanus and Diptheria Toxoids Adsorbed manufactured by Sanofi Pasteur, Limited). Blood samples for immunogenicity analyses were obtained from participants pre-vaccination and approximately 28 days post-vaccination. The pre-vaccination antibody concentration was used for all immunogenicity analyses, and included 948 participants in the Adacel group and 317 participants in the Td control vaccine group. Of the study participants, 35% were male. Of subjects who reported a racial/ethnic demographic, 95% were Caucasian, 2% Black, 0.5% American Indian or Alaska Native, 1% Asian and 1.5% were of mixed or other origin.

A tetanus toxoid antigen level of ≥0.1 IU/mL was measured by the ELISA used in this study was considered protective. An anti-diphtheria anti-toxin level of ≥0.1 IU/mL was considered protective. Pre-vaccination and post-vaccination seroprotection rates and booster response rates are presented in Table 8.

Table 9: Ratio of Pertussis Antibody Geometric Mean Concentrations (GMCs) Observed One Month Following a Second Vaccination with Adacel in Adults Compared to Those Observed in Infants One Month Following Vaccination with 3 or 4 Doses of DAPTACEL (Per-Protocol Analysis Set)

Table 8: Pre-vaccination and Post-vaccination Seroprotection Rates and Booster Response Rates to Tetanus Toxoid and Diptheria Toxoid Following a Second Vaccination with Adacel Compared to Td Vaccine in Persons 18 through 64 Years of Age, Per Protocol Analysis Set

For all pertussis antigens (PT, FHA, PRN, and FIM), post-vaccination anti-pertussis GMCs in the Adacel group were non-inferior to GMCs induced by 3 or 4 doses of DAPTACEl in historical studies as are presented in Table 9.
15 REFERENCES
5 FDA, Department of Health and Human Services (DHHS). Biological products bacterial vaccines and toxoids; implementation of efficacy review; proposed rule. Fed Reg 1985;50(240):51002-117.

16 HOW SUPPLIED/STORAGE AND HANDLING
Syringe, without needle, single-dose – NDC 49281-400-89 (not made with natural rubber latex); in package of 5 syringes, NDC 49281-400-20.
Syringe, without needle, single-dose – NDC 49281-400-88; in package of 5 syringes, NDC 49281-400-15. The tip caps of the prefilled syringes may contain natural rubber latex. No other components are made with natural rubber latex.
Vial, single-dose – NDC 49281-400-58; in package of 5 vials; NDC 49281-400-05. The vial stopper is not made with natural rubber latex. Discard unused portion in vial.
Vial, single-dose – NDC 49281-400-56; in package of 10 vials; NDC 49281-400-10. The vial stopper is not made with natural rubber latex. Discard unused portion in vial.
Not all pack sizes may be marketed.
Adacel 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.

17 PATIENT COUNSELING INFORMATION
Before administration of Adacel, healthcare providers should inform the patient, parent or guardian of the benefits and risks of the vaccine and the importance of receiving recommended booster dose unless a contraindication to further immunization exists.
The healthcare provider should inform the patient, parent or guardian about the potential for adverse reactions that have been temporally associated with Adacel or other vaccines containing similar components. The healthcare provider should provide the Vaccine Information Statements (VISs) that are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization. The patient, parent or guardian should be instructed to report any serious adverse reactions to their healthcare provider.
Pregnancy Exposure Registry
[See USE IN SPECIFIC POPULATIONS (8.1).]
Manufactured by:
Sanofi Pasteur Limited
Toronto Ontario Canada

Distributed by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

Adacel® is a registered trademark of Sanofi, its affiliates, and its subsidiaries.

R12-0120 USA
TRDP-FPLR-SL-JAN20 Rx Only