**CONTRAINDICATIONS**

Suspension for injection, supplied in single dose (0.5 mL) vials. (3)

A single intramuscular injection of 0.5 mL. (2)

**DOSAGE AND ADMINISTRATION**

Quadracel is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis. A single dose of Quadracel is approved for use in children 4 through 6 years of age as a fifth dose in the diphtheria, tetanus, pertussis vaccination (DTPa) series, and as a fourth or fifth dose in the inactivated poliovirus vaccination (IPV) series, in children who have received 4 doses of Pentacel and/or DAPTACEL vaccine. (1)

**DOSE AND ADMINISTRATION**

A single intramuscular injection of 0.5 mL. (2)

**DOSAGE FORMS AND STRENGTHS**

Suspension for injection, supplied in single dose (0.5 mL) vials. (3)

**CONTRAINDICATIONS**

- Severe allergic reaction (e.g., anaphylaxis) to any ingredient of Quadracel or following any diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine or inactivated poliovirus vaccine. (4.1) (11)
- Encephalopathy within 7 days of a previous pertussis-containing vaccine with no other identifiable cause. (4.2)

**INDICATIONS AND USAGE**

Quadracel is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis. A single dose of Quadracel is approved for use in children 4 through 6 years of age as a fifth dose in the diphtheria, tetanus, pertussis vaccination (DTPa) series, and as a fourth or fifth dose in the inactivated poliovirus vaccination (IPV) series, in children who have received 4 doses of Pentacel and/or DAPTACEL vaccine. (1)

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

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

**Quadracel (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine)**

Suspension for Intramuscular Injection

Initial U.S. Approval: 2015

**INDICATIONS AND USAGE**

Initial U.S. Approval: 2015

**CONTRAINDICATIONS**

- Severe allergic reaction (e.g., anaphylaxis) to any ingredient of Quadracel [see Description (17)], or following any diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, or inactivated poliovirus vaccine, is a contraindication to administration of Quadracel.
- Progressive neurologic disorder until a treatment regimen has been established and the condition has stabilized. (4.3)
- Carefully consider benefits and risks before administering Quadracel to persons with a history of:
  - Fever >40.5°C (≥105°F), hypotonic-hyporesponsive episode (HHE) or persistent, inconsolable crying lasting ≥23 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 Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including Quadracel, should be based on careful consideration of the potential benefits and possible risks. (5.3)

**ADVERSE REACTIONS**

In a clinical study, the most common solicited injection site reactions were pain (>75%), increase in arm circumference (>65%), erythema (>55%), and swelling (>40%). Common solicited systemic reactions were myalgia (>50%), malaise (>35%), and headache (>15%). (6.1)

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

See 17 for PATIENT COUNSELING INFORMATION

Revised: 02/2021

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2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
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5 WARNINGS AND PRECAUTIONS
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**FULL PRESCRIBING INFORMATION**

1 INDICATIONS AND USAGE

Quadracel® is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis. A single dose of Quadracel is approved for use in children 4 through 6 years of age as a fifth dose in the diphtheria, tetanus, pertussis vaccination (DTPa) series, and as a fourth or fifth dose in the inactivated poliovirus vaccination (IPV) series, in children who have received 4 doses of Pentacel® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus and Haemophilius b conjugate [Tetanus Toxoid Conjugate Vaccine] and/or DAPTACEL® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed]).

2 DOSAGE AND ADMINISTRATION

For intramuscular use only.

Just before use, shake the vial well, until a uniform, white, cloudy suspension results. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exist, the product should not be administered.

Using a sterile needle and syringe and aseptic technique, withdraw and administer a 0.5 mL dose of Quadracel vaccine intramuscularly into the deltoid muscle of the upper arm. Discard unused portion.

Quadracel should not be combined through reconstitution or mixed with any other vaccine.

3 DOSAGE FORMS AND STRENGTHS

Quadracel is a suspension for injection in 0.5 mL single-dose vials.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Severe allergic reaction (e.g., anaphylaxis) to any ingredient of Quadracel [see Description (17)] or following any diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, or inactivated poliovirus vaccine, is a contraindication to administration of Quadracel.
In a clinical study, the most common solicited injection site reactions were pain (>75%), increase in arm circumference (>40%), erythema (>55%), and swelling (>40%). Common solicited systemic reactions were myalgia (>50%), malaise (>35%), and headache (>15%).

6. ADVERSE REACTIONS

In a clinical study, the most common solicited injection site reactions were pain (>75%), increase in arm circumference (>40%), erythema (>55%), and swelling (>40%). Common solicited systemic reactions were myalgia (>50%), malaise (>35%), and headache (>15%).

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.

In a randomized, controlled, multicenter study conducted in the US and Puerto Rico (Study M5I02; ClinicalTrials.gov Identifier: NCT01346293), 3,372 children, 4 to 6 years of age, who had received 4 doses of DAPTACEL and/or Pentacel vaccine(s) received Quadracel, or DAPTACEL + IPOL (Poliovirus Vaccine Inactivated) vaccines administered concomitantly, or DAPTACEL + IPOL vaccines administered concomitantly at separate sites. Subjects also received Measles, Mumps, and Rubella Virus Vaccine Live (MMR) (Merck & Co., Inc.) and Varicella Virus Vaccine Live (Varicella vaccine) (Merck & Co., Inc.) administered concomitantly at separate sites. Safety was evaluated in 2,733 subjects who received Quadracel and 621 subjects who received DAPTACEL + IPOL vaccines.

Among these subjects, 51.5% were male, 48.5% were female, 75.7% were Caucasian, 8.6% were Black, 7.9% were Hispanic, 0.9% were Asian, and 7.8% were of other racial/ethnic groups. The mean age for both groups was 4.4 years and the ratio of male to female subjects and ethnicity were balanced between both groups. Solicited injection site reactions and systemic reactions were collected daily for 7 days following vaccination, via diary cards. Participants were monitored for unsolicited adverse events for 28 days and serious adverse events (SAEs) for 6 months after vaccination.

Solicited Adverse Reactions

The incidence and severity of solicited injection site and systemic adverse reactions that occurred within 7 days after vaccination in each study group are shown in Table 1.

### Table 1: Percentage of Children 4 through 6 Years of Age with Solicited Adverse Reactions by Intensity Within 7 Days of Vaccination with Quadracel or Concomitant but Separate DAPTACEL and IPOL vaccines Co-Administered with MMR and Varicella Vaccines

<table>
<thead>
<tr>
<th>Category</th>
<th>Quadracel (N = 2,500-2,689)</th>
<th>DAPTACEL + IPOL (N = 598-603)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site Reactions</td>
<td>Quadracel site</td>
<td>DAPTACEL or IPOL site</td>
</tr>
<tr>
<td>Pain</td>
<td>Any</td>
<td>77.4</td>
</tr>
<tr>
<td></td>
<td>Grade 1</td>
<td>56.4</td>
</tr>
<tr>
<td></td>
<td>Grade 2</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>2.0</td>
</tr>
<tr>
<td>Change in limb circumference</td>
<td>Any</td>
<td>68.1</td>
</tr>
<tr>
<td></td>
<td>Grade 1</td>
<td>59.8</td>
</tr>
<tr>
<td></td>
<td>Grade 2</td>
<td>8.2</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>0.2</td>
</tr>
<tr>
<td>Erythema</td>
<td>Any</td>
<td>59.1</td>
</tr>
<tr>
<td></td>
<td>&gt;0 to &lt;25 mm</td>
<td>31.6</td>
</tr>
<tr>
<td></td>
<td>≥25 to &lt;50 mm</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td>≥50 mm</td>
<td>18.0</td>
</tr>
<tr>
<td>Swelling</td>
<td>Any</td>
<td>40.2</td>
</tr>
<tr>
<td></td>
<td>&gt;0 to &lt;25 mm</td>
<td>23.5</td>
</tr>
<tr>
<td></td>
<td>≥25 to &lt;50 mm</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>≥50 mm</td>
<td>8.6</td>
</tr>
<tr>
<td>Extensive limb swelling</td>
<td>Any</td>
<td>1.5</td>
</tr>
<tr>
<td>Systemic Reactions</td>
<td>Any</td>
<td>53.8</td>
</tr>
<tr>
<td></td>
<td>Grade 1</td>
<td>36.0</td>
</tr>
<tr>
<td></td>
<td>Grade 2</td>
<td>15.8</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>1.9</td>
</tr>
</tbody>
</table>

*ClinicalTrials.gov Identifier: NCT01346293.
†N = The number of subjects with available data.
‡Grade 1: Easily tolerated. Grade 2: Sufficiently discomforting to interfere with normal behavior or activities. Grade 3: Incapacitating, unable to perform usual activities. Grade 4: Severe, incapacitating, life-threatening.
## Serious Adverse Events

In Study M5I02, within 28 days following vaccination with Quadracel, or DAPTACEL + IPOL vaccines, and concomitant MMR and varicella vaccines, 0.1% of subjects (3/2,733) in the Quadracel group experienced a serious adverse event. During the same time period, 0.2% of subjects (1/621) in the DAPTACEL + IPOL group experienced a SAE. Within the 6-month follow-up period after vaccination, SAEs were reported in 0.8% of subjects (21/2,733) who received Quadracel and 0.5% of subjects (3/621) who received DAPTACEL + IPOL vaccines, none of which were assessed as related to vaccination.

## 7. DRUG INTERACTIONS

**7.1 Concomitant Administration with Other Vaccines**

In the US clinical trial, Study M5I02, Quadracel was administered concomitantly with one or more of the following US-licensed vaccines: MMR vaccine and varicella vaccine. [See Adverse Reactions (6.1).]

When Quadracel is given at the same time as another injectable vaccine(s), the vaccines 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 Quadracel. [See Warnings and Precautions (5.5).]
8 USE IN SPECIFIC POPULATIONS
8.4 Pediatric Use
The safety and effectiveness of Quadracel has not been established in children less than 4 years of age or children 7 through 16 years of age and is not approved for use in these age groups.

11 DESCRIPTION
Quadracel (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) is a sterile suspension for intramuscular injection. Each 0.5 mL dose is formulated to contain 15 L diphtheria toxoid, 5 L tetanus toxoid, acellular pertussis antigens (PT, FHA, PRN, 20 mcg filamentous hemagglutinin (FHA), 3 mcg pertactin (PRN), 5 mcg fimbriae types 2 and 3 (FIM)), and inactivated polioviruses [40 D-antigen units (DU) Type 1 (Mahoney), 8 DU Type 2 (MEP-1), 32 DU Type 3 (Saukett)].

Corynebacterium diphtheriae is grown in modified Mueller's growth medium. After clarification and filtration, the bacterial culture medium is replaced by Medium 199, without 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 the monovalent viral suspensions are inactivated with formaldehyde. Monovalent concentrates of each inactivated poliovirus are combined to produce a trivalent poliovirus concentrate. The adsorbed diphtheria, tetanus and acellular pertussis antigens are combined with aluminum phosphate, 2-phenoxethanol (not as a preservative) and water for injection, into an intermediate concentrate. The trivalent poliovirus concentrate is added and the vaccine is diluted to its final concentration.

Each 0.5 mL dose contains 1.5 mg aluminum phosphate (0.33 mg aluminum) as the adjuvant, polysorbate 80 (approximately 10 ppm by calculation), ≤2 mcg residual formaldehyde, ≤50 ng residual glutaraldehyde, ≤50 ng residual bovine serum albumin, 3.3 mg (0.6% w/v) 2-phenoyethanol (not as a preservative), ≤4 pg of neomycin and ≤4 pg polymyxin B sulfate.

Quadracel 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 mice to detoxified PT, FHA, PRN and FIM as measured by enzyme-linked immunosorbent assay (ELISA). The potency of the inactivated poliovirus antigens is determined by measuring antibody-mediated neutralization of poliovirus in sera from immunized rats.

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 <4 pg of neomycin and ≤4 pg polymyxin B sulfate.

Quadracel contains twice as much detoxified PT and four times the neomycin and ≤4 pg polymyxin B sulfate.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Quadracel has not been evaluated for carcinogenic or mutagenic potential or impairment of fertility.
Table 3: Booster Response Rates and Post-vaccination Antibody Levels to Pertussis Antigens Following Quadracel or Concomitant but Separate DAPTACEL and IPOL Vaccines Co-Administered with MMR and Varicella Vaccines (continued)

<table>
<thead>
<tr>
<th>Anti-PRN</th>
<th>Quadracel (N: 250-255)</th>
<th>DAPTACEL + IPOL (N: 247-249)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Booster Response</td>
<td>96.6</td>
<td>93.1</td>
</tr>
<tr>
<td>Post-vaccination GMC (EU/mL)</td>
<td>282.6</td>
<td>187.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anti-FIM</th>
<th>Quadracel (N: 247-258)</th>
<th>DAPTACEL + IPOL (N: 248-253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Booster Response</td>
<td>97.2</td>
<td>92.4</td>
</tr>
<tr>
<td>Post-vaccination GMC (EU/mL)</td>
<td>505.8</td>
<td>378.9</td>
</tr>
</tbody>
</table>

*ClinicalTrials.gov Identifier: NCT01346293.
†N = The number of subjects with available data.
‡Booster response: In subjects with pre-vaccination antibody concentrations <LLOQ, a post-vaccination level ≥4×LLOQ; in subjects with pre-vaccination antibody concentrations ≥LLOQ but <4×LLOQ, a 4-fold rise in post-vaccination level; in subjects with pre-vaccination antibody level ≥4×LLOQ, a 2-fold rise in post-vaccination level.
§Quadracel was non-inferior to DAPTACEL + IPOL based on the post-vaccination booster response rates for all pertussis antigens (lower limits of the 2-sided 95% CIs of the difference [Quadracel minus DAPTACEL + IPOL] were >-10%).
¶Quadracel was non-inferior to DAPTACEL + IPOL based on the post-vaccination GMTs for all pertussis antigens (lower limits of the 2-sided 95% CIs of the ratio [Quadracel / DAPTACEL + IPOL] were >23).

Table 4: Booster Response Rates, Pre- and Post-Vaccination Seroprotection Rates and Post-vaccination Antibody Levels to Poliovirus Antigens Following Quadracel or Concomitant but Separate DAPTACEL and IPOL Vaccines Co-Administered with MMR and Varicella Vaccines

<table>
<thead>
<tr>
<th>Anti-Poliovirus 1</th>
<th>Quadracel (N: 247-258)</th>
<th>DAPTACEL + IPOL (N: 248-253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Booster Response</td>
<td>85.9</td>
<td>82.3</td>
</tr>
<tr>
<td>Pre-vaccination % ≥1:8 dilution</td>
<td>98.4</td>
<td>98.8</td>
</tr>
<tr>
<td>Post-vaccination % ≥1:8 dilution</td>
<td>100.0</td>
<td>99.6</td>
</tr>
<tr>
<td>Post-vaccination GMT</td>
<td>3,477</td>
<td>2,731</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anti-Poliovirus 2</th>
<th>Quadracel (N: 247-258)</th>
<th>DAPTACEL + IPOL (N: 248-253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Booster Response</td>
<td>78.3</td>
<td>79.0</td>
</tr>
<tr>
<td>Pre-vaccination % ≥1:8 dilution</td>
<td>99.6</td>
<td>99.6</td>
</tr>
<tr>
<td>Post-vaccination % ≥1:8 dilution</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Post-vaccination GMT</td>
<td>3,491</td>
<td>3,894</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anti-Poliovirus 3</th>
<th>Quadracel (N: 247-258)</th>
<th>DAPTACEL + IPOL (N: 248-253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Booster Response</td>
<td>85.0</td>
<td>84.7</td>
</tr>
<tr>
<td>Pre-vaccination % ≥1:8 dilution</td>
<td>96.8</td>
<td>93.1</td>
</tr>
<tr>
<td>Post-vaccination % ≥1:8 dilution</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Post-vaccination GMT</td>
<td>4,591</td>
<td>3,419</td>
</tr>
</tbody>
</table>

*ClinicalTrials.gov Identifier: NCT01346293.
†N = The number of subjects with available data.
‡Booster response: In subjects with pre-vaccination antibody concentrations <1:8 dilution, post-vaccination levels ≥1:8 dil; in subjects with pre-vaccination antibody concentrations ≥1:8 dilution, a 4-fold rise in post-vaccination antibody levels.
§Quadracel was non-inferior to DAPTACEL + IPOL based on the post-vaccination booster response rates for polio types 1, 2 and 3 (lower limits of the 2-sided 95% CIs of the difference [Quadracel minus DAPTACEL + IPOL] were >-10%).
¶Quadracel was non-inferior to DAPTACEL + IPOL based on the post-vaccination GMTs for polio types 1, 2 and 3 (lower limits of the 2-sided 95% CIs of the ratio [Quadracel / DAPTACEL + IPOL] were >23).

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
The vial stopper for this product is not made with natural latex rubber. Quadracel is supplied in a single-dose vial (NDC No. 49218-562-58) in packages of 10 vials (NDC No. 49218-562-10).

16.2 Storage and Handling
Quadracel 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
Inform the parent or guardian of the following:
• The potential benefits and risks of immunization with Quadracel.
• The common adverse reactions that have occurred following administration of Quadracel or other vaccines containing similar components.
• Other adverse reactions can occur. Call healthcare provider with any adverse reactions of concern.

Provide the Vaccine Information Statements (VIS), which are required by the National Childhood Vaccine Injury Act of 1986.

Manufactured by:
Sanofi Pasteur Limited
Toronto Ontario Canada

Distributed by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

Quadracel® is a registered trademark of Sanofi Pasteur Limited.

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