Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

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----------

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 (DTaP) 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)

----------DOSAGE 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)
- 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 Quadracel to persons with a history of:
  - fever ≥40.5°C (≥105°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)
- 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: 01/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

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

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 (DTaP) 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 *Haemophilus* 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.

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 (11)*] or following any diphtheria toxoid, tetanus toxoid, pertussis-containing vaccine, or inactivated poliovirus vaccine, is a contraindication to administration of Quadracel.

4.2 Encephalopathy

Encephalopathy (e.g., 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 Quadracel.

4.3 Progressive Neurologic Disorder

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

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

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

5.2 Adverse Reactions Following Prior Pertussis Vaccination

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

- Temperature of ≥40.5°C (≥105°F) within 48 hours, not attributable to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode [HHE]) 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

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.

5.4 Limitations of Vaccine Effectiveness

Vaccination with Quadracel may not protect all individuals.

5.5 Altered Immunocompetence

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

6 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 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), 3372 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 but 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 2733 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*

		Quadracel (N† = 2500-2689)	DAPTACEL + IPOL (N† = 598-603)
Injection Site Reactions		Quadracel site	DAPTACEL or IPOL site
Pain‡	Any	77.4	76.5
	Grade 1	56.4	54.9
	Grade 2	19.0	18.6
	Grade 3	2.0	3.0
Change in limb circumference§	Any	68.1	65.1
	Grade 1	59.8	58.6
	Grade 2	8.2	6.5
	Grade 3	0.2	0.0
Erythema	Any	59.1	53.4
	> 0 to < 25 mm	31.6	31.8
	≥ 25 to < 50 mm	9.5	9.6
	≥ 50 mm	18.0	11.9
Swelling	Any	40.2	36.4
	> 0 to < 25 mm	23.5	23.1
	≥ 25 to < 50 mm	8.1	6.1
	≥ 50 mm	8.6	7.1
Extensive limb swelling¶	Any	1.5	1.3
Systemic Reactions			
Myalgia#	Any	53.8	52.6
	Grade 1	36.0	33.5
	Grade 2	15.8	16.3
	Grade 3	1.9	2.8
Malaise#	Any	35.0	33.2
	Grade 1	21.7	18.7
	Grade 2	10.6	11.1
	Grade 3	2.6	3.3
Headache#	Any	15.6	16.6
	Grade 1	11.9	11.9
	Grade 2	3.1	4.0
	Grade 3	0.6	0.7
Fever	Any	6.0	6.9
	≥ 38.0°C to ≤ 38.4°C	2.6	3.0
	≥ 38.5°C to ≤ 38.9°C	2.1	1.8
	≥ 39.0°C	1.3	2.0

* 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 1: > 0 to < 25 mm increase over pre-vaccination measurement, Grade 2: ≥ 25 to ≤ 50 mm increase over pre-vaccination measurement, Grade 3: > 50 mm increase over pre-vaccination measurement.

[¶] Swelling of the injected limb including the adjacent joint (i.e., elbow and/or shoulder) as compared to baseline.

[#] Grade 1: No interference with activity, Grade 2: Some interference with activity, Grade 3: Significant; prevents daily activity.

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 (3/2733) in the Quadracel group experienced a serious adverse event. During the same time period, 0.2% 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 (21/2733) who received Quadracel and 0.5% of subjects (3/621) who received DAPTACEL + IPOL vaccines, none of which were assessed as related to vaccination.

6.2 Postmarketing Experience

The following adverse events have been spontaneously reported, during the post-marketing use of Quadracel outside the US, in infants and children from 2 months through 6 years of age. Because these events are reported voluntarily from a population of uncertain size, it is not possible to estimate their frequency reliably or establish a causal relationship to vaccine exposure. This list includes adverse events based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to Quadracel.

Immune system disorders

Anaphylactic reaction, hypersensitivity and allergic reactions (such as rash, urticaria, dyspnea)

Psychiatric disorders

Screaming

Nervous system disorders

Somnolence, convulsion, febrile convulsion, HHE, hypotonia

Cardiac disorders

Cyanosis

Vascular disorders

Pallor

General disorders and administration site conditions

Listlessness

Injection site reactions (including inflammation, mass, sterile abscess, and edema)

Large injection site reactions (>50 mm), including limb swelling which may extend from the injection site beyond one or both joints

Infections and Infestations

Injection site cellulitis, injection site abscess

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

8.1 Pregnancy

Quadracel is not approved for use in individuals 7 years of age and older. No human or animal data are available to assess vaccine-associated risks in pregnancy.

8.2 Lactation

Quadracel is not approved for use in individuals 7 years of age and older. No human or animal data are available to assess the impact of Quadracel on milk production, its presence in breast milk, or its effects on the breastfed infant.

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 Adsorbed and Inactivated Poliovirus Vaccine) is a sterile suspension for intramuscular injection.

Each 0.5 mL dose is formulated to contain 15 Lf diphtheria toxoid, 5 Lf tetanus toxoid, acellular pertussis antigens [20 mcg detoxified pertussis toxin (PT), 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 (MEF-1), 32 DU Type 3 (Saukett)].

Corynebacterium diphtheriae is grown in modified Mueller's growth medium. (1) After purification by ammonium sulfate fractionation, the diphtheria toxin is detoxified with formaldehyde and diafiltered.

Clostridium tetani is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (2) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulfate fractionation and diafiltration. Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate.

The acellular pertussis vaccine antigens are produced from *Bordetella pertussis* cultures grown in Stainer-Scholte medium (3) modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. PT, FHA and PRN are isolated separately from the supernatant culture medium. FIM are extracted and copurified from the bacterial cells. The pertussis antigens are purified by sequential filtration, salt-precipitation, ultrafiltration and chromatography. PT is detoxified with glutaraldehyde. FHA is treated with formaldehyde and the residual aldehydes are removed by ultrafiltration. The individual antigens are adsorbed separately onto aluminum phosphate.

Poliovirus Type 1, Type 2 and Type 3 are each grown in separate cultures of MRC-5 cells, a line of normal human diploid cells, by the microcarrier method. (4) (5) The cells are grown in CMRL (Connaught Medical Research Laboratories) 1969 medium, supplemented with calf serum. For viral growth, the culture medium is replaced by Medium 199, without calf serum. After clarification and filtration, the viral suspensions are concentrated by ultrafiltration, and purified by liquid chromatography steps. The 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-phenoxyethanol (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), ≤5 mcg residual formaldehyde, <50 ng residual glutaraldehyde, ≤50 ng residual bovine serum albumin, 3.3 mg (0.6% v/v) 2-phenoxyethanol (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 some degree

of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. (6) Levels of 1.0 IU/mL have been associated with long-term protection. (7)

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. (6) (8). A tetanus antitoxoid level ≥0.1 IU/mL as measured by the ELISA used in clinical studies of Quadracel is considered protective.

Pertussis

Pertussis (whooping cough) is a respiratory disease caused by *B. pertussis*. This Gram-negative coccobacillus produces a variety of biologically active components, though their role in either the pathogenesis of, or immunity to, pertussis has not been clearly defined.

There is no well-established serological correlate of protection for pertussis. Because DAPTACEL contains the same pertussis antigens manufactured by the same process as those in Quadracel, the effectiveness of Quadracel against pertussis was based on a comparison of pertussis immune responses following Quadracel to those following DAPTACEL (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed). [See *Clinical Studies (14)*]. The efficacy of the pertussis component of DAPTACEL was determined in clinical trials of DAPTACEL administered to infants (see DAPTACEL prescribing information). Quadracel contains twice as much detoxified PT and four times as much FHA as DAPTACEL.

Poliomyelitis

Polioviruses, of which there are three serotypes (Types 1, 2, and 3), are enteroviruses. The presence of poliovirus type-specific neutralizing antibodies has been correlated with protection against poliomyelitis. (9)

13 NON-CLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

14 CLINICAL STUDIES

14.1 Immunogenicity

In Study M5I02, children 4 through 6 years of age received Quadracel or DAPTACEL + IPOL as the fifth dose in the diphtheria, tetanus, and pertussis vaccination series and the fourth or fifth dose in the inactivated poliovirus vaccination series. Subjects also received their second dose of MMR and Varicella vaccines, concomitantly. The immunogenicity subset comprised 263 subjects in the Quadracel group and 253 subjects in the DAPTACEL + IPOL vaccines group. [See study description in *Adverse Reactions (6.1)*].

Antibody levels to diphtheria, tetanus, pertussis (PT, FHA, PRN and FIM) and poliovirus antigens were measured in sera obtained immediately prior to vaccination and 28 days after vaccination. The co-primary endpoints were booster response rates and antibody geometric mean concentrations/titers (GMCs/GMTs) to diphtheria, tetanus, pertussis and poliovirus antigens elicited after vaccination. Booster response rates and antibody GMCs/GMTs following Quadracel vaccination were compared to those after DAPTACEL + IPOL vaccination.

Quadracel was non-inferior to DAPTACEL + IPOL vaccines administered concomitantly at separate sites, as demonstrated by comparison of the post-vaccination antibody booster response rates and GMCs/GMTs to diphtheria and tetanus (Table 2), to all pertussis antigens (Table 3) and to poliovirus 1, 2 and 3 (Table 4).

Table 2: Booster Response Rates, Pre- and Post-Vaccination Seroprotection Rates and Post-Vaccination Antibody Levels to Diphtheria and Tetanus Antigens Following Quadracel or Concomitant but Separate DAPTACEL and IPOL Vaccines Co-Administered with MMR and Varicella Vaccines*

	Quadracel (N† =253-262)	DAPTACEL + IPOL (N† =248-253)
Anti-Diphtheria		
% Booster Response‡	97.3§	99.2
Pre-vaccination % ≥0.1 IU/mL¶	90.7	83.1
Post-vaccination % ≥0.1 IU/mL¶	100.0	99.6
Post-vaccination % ≥1.0 IU/mL¶	99.6	99.6
Post-vaccination GMC (IU/mL)	18.6#	15.5
Anti-Tetanus		
% Booster Response‡	84.2§	84.3
Pre-vaccination % ≥0.1 IU/mL¶	91.7	89.1
Post-vaccination % ≥0.1 IU/mL¶	100.0	99.2
Post-vaccination % ≥1.0 IU/mL¶	98.9	96.8
Post-vaccination GMC (IU/mL)	6.4#	5.5

* ClinicalTrials.gov Identifier: NCT01346293.

† N = The number of subjects with available data.

‡ Booster response: In subjects with pre-vaccination antibody concentrations < 0.1 IU/mL, a post-vaccination level ≥ 0.4 IU/mL; in subjects with pre-vaccination antibody concentrations ≥ 0.1 IU/mL but < 2.0 IU/mL, a 4-fold rise in post-vaccination level; in subjects with pre-vaccination antibody level ≥ 2.0 IU/mL, a 2-fold rise in post-vaccination level.

§ Quadracel was non-inferior to DAPTACEL + IPOL based on the post-vaccination booster response rates for diphtheria and tetanus (lower limits of the 2-sided 95% CIs of the difference [Quadracel minus DAPTACEL + IPOL] were >-10%).

¶ Seroprotection: anti-diphtheria and anti-tetanus antibody concentrations ≥ 0.1 IU/mL and ≥ 1.0 IU/mL.

Quadracel was non-inferior to DAPTACEL + IPOL based on the post-vaccination GMCs for diphtheria and tetanus (lower limits of the 2-sided 95% CIs of the ratio [Quadracel / DAPTACEL + IPOL] were > 2/3).

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*

	Quadracel (N† =250-255)	**DAPTACEL + IPOL (N† =247-249)**
Anti-PT		
% Booster Response‡	95.2§	89.9
Post-vaccination GMC (EU/mL)	120.7¶	61.3
Anti-FHA		
% Booster Response‡	94.9§	87.5
Post-vaccination GMC (EU/mL)	123.5¶	79.0
Anti-PRN		
% Booster Response‡	96.9§	93.1
Post-vaccination GMC (EU/mL)	282.6¶	187.5
Anti-FIM		
% Booster Response‡	97.2§	92.4
Post-vaccination GMC (EU/mL)	505.8¶	378.9

* 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 ≥ 4xLLOQ; in subjects with pre-vaccination antibody concentrations ≥ LLOQ but < 4xLLOQ, a 4-fold rise in post-vaccination level; in subjects with pre-vaccination antibody level ≥ 4xLLOQ, 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 GMCs for all pertussis antigens (lower limits of the 2-sided 95% CIs of the ratio [DTaP-IPV / DAPTACEL + IPOL] were > 2/3).

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*

	Quadracel (N† =247-258)	DAPTACEL + IPOL (N† =248-253)
Anti-Poliovirus 1		
% Booster Response‡	85.9§	82.3
Pre-vaccination % ≥1:8 dilution	98.4	98.8
Post-vaccination % ≥1:8 dilution	100.0	99.6
Post-vaccination GMT	3477¶	2731
Anti-Poliovirus 2		
% Booster Response‡	78.3§	79.0
Pre-vaccination % ≥1:8 dilution	99.6	99.6
Post-vaccination % ≥1:8 dilution	100.0	100.0
Post-vaccination GMT	3491¶	3894
Anti-Poliovirus 3		
% Booster Response‡	85.0[d]	84.7
Pre-vaccination % ≥1:8 dilution	96.8	93.1
Post-vaccination % ≥1:8 dilution	100.0	100.0
Post-vaccination GMT	4591¶	3419

* 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 > 2/3).

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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. 49281-562-58) in packages of 10 vials (NDC No. 49281-562-10).

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

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