HIGHLIGHTS OF PRESCRIBING INFORMATION

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

TENIVAC (Tetanus and Diphtheria Toxoids Adsorbed)
Suspension for Intramuscular Injection
Initial US Approval: 2003

----------INDICATIONS AND USAGE----------

- TENIVAC is a vaccine indicated for active immunization for the prevention of tetanus and diphtheria in persons 7 years of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------

- Each 0.5 mL dose should be administered intramuscularly. (2.5)
- Primary immunization with TENIVAC consists of 3 doses. The first 2 doses are administered 2 months apart and the third dose is administered 6-8 months after the second dose. (2.1)
- TENIVAC may be used for booster immunization against tetanus and diphtheria. Routine booster immunization against tetanus and diphtheria is recommended at 11-12 years of age and every 10 years thereafter. (2.2)
- For post-exposure diphtheria prophylaxis and for management of a tetanus prone wound, a booster dose of TENIVAC may be administered if at least 5 years have elapsed since previous receipt of a diphtheria toxoid and tetanus toxoid containing vaccine. (2.3) (2.4)

----------DOSAGE FORMS AND STRENGTHS----------

- Suspension for injection supplied in 0.5 mL single-dose vials or syringes. (3)

----------CONTRAINDICATIONS----------

- Severe allergic reaction (e.g., anaphylaxis) to a previous dose of TENIVAC, or any other tetanus or diphtheria toxoid-containing vaccine, or any component of this vaccine. (4.1)

----------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)
- More frequent administration of TENIVAC than described in Dosage and Administration (2.1, 2.2, 2.3, 2.4) may be associated with increased incidence and severity of adverse reactions. (5.3)
- Persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine should not receive TENIVAC more frequently than every 10 years, even for tetanus prophylaxis as part of wound management. (5.4)
- Carefully consider benefits and risks before administering TENIVAC to persons with a history of Guillain-Barré syndrome within 6 weeks of a previous tetanus toxoid-containing vaccine. (5.5)

----------ADVERSE REACTIONS----------

- The most frequent solicited injection site reaction within 0-3 days following TENIVAC was pain, reported in 78.3% of study participants 11-59 years of age and 35.3% of participants ≥60 years of age. (6.1)
- The most frequent solicited systemic reaction within 0-3 days following TENIVAC was headache, reported in 17.9% of participants, overall. (6.1)
- Other common (≥10%) solicited adverse reactions within 0-3 days following TENIVAC were injection site redness, injection site swelling, malaise, muscle weakness and pain in joints. (6.1)

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

----------DRUG INTERACTIONS----------

- No safety and immunogenicity data are available on the concomitant administration of TENIVAC with other US licensed vaccines. (7.1)
- If passive protection against tetanus is required, Tetanus Immune Globulin (TIG) (Human) may be administered concomitantly at a separate site with a separate needle and syringe. (7.2)
- Immunosuppressive therapies may reduce the immune response to TENIVAC. (7.3)

----------USE IN SPECIFIC POPULATIONS----------

Pre- and post-vaccination tetanus and diphtheria seroprotection rates were lower in study participants ≥65 years of age compared to younger participants. In general, rates of solicited adverse reactions were not higher in participants ≥65 years of age compared to younger participants. (8.5)

See 17 for **PATIENT COUNSELING INFORMATION**

Revised: [April 2013]

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TENIVAC® is a vaccine indicated for active immunization for the prevention of tetanus and diphtheria in persons 7 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Primary Immunization

In persons who have not been immunized previously against tetanus and diphtheria, primary immunization with TENIVAC vaccine consists of three 0.5 mL doses. The first 2 doses are administered 2 months apart and the third dose is administered 6-8 months after the second dose.

TENIVAC vaccine may be used to complete the primary immunization series for tetanus and diphtheria, following one or two doses of Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (whole-cell DTP), Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP), and/or Diphtheria and Tetanus Toxoids Adsorbed (DT). However, the safety and efficacy of TENIVAC vaccine in such regimens have not been evaluated.

2.2 Routine Booster Immunization

TENIVAC vaccine may be used for routine booster immunization against tetanus and diphtheria in persons 7 years of age and older. Routine booster immunization against tetanus and diphtheria is recommended in children 11-12 years of age and every 10 years thereafter.

2.3 Diphtheria Prophylaxis for Case Contacts

TENIVAC vaccine may be used for post-exposure diphtheria prophylaxis in persons 7 years of age and older who have not completed primary vaccination, whose vaccination status is unknown, or who have not been vaccinated with diphtheria toxoid within the previous 5 years. Consult recommendations of the Advisory Committee on Immunization Practices for additional interventions for diphtheria prophylaxis in close contacts of diphtheria patients. (1)

2.4 Tetanus Prophylaxis in Wound Management

For active tetanus immunization in wound management of patients 7 years of age and older, a preparation containing tetanus and diphtheria toxoids is preferred instead of single-antigen tetanus toxoid to enhance diphtheria protection. (1) TENIVAC vaccine is approved for wound management of patients 7 years of age and older.

The need for active immunization with a tetanus toxoid-containing preparation, with or without passive immunization with Tetanus Immune Globulin (TIG) (Human) depends on both the condition of the wound and the patient's vaccination history. (See Table 1.)

When indicated, TIG (Human) should be administered at a separate site, with a separate needle and syringe, according to the manufacturer's package insert. If a contraindication to using tetanus toxoid-containing preparations exists in a person who has not completed a primary immunizing course of tetanus toxoid and other than a clean, minor wound is sustained, only passive immunization with TIG (Human) should be given. (1)

Table 1: Guide for use of Tetanus and Diphtheria Toxoids Adsorbed (Td) for Tetanus Prophylaxis in Routine Wound Management in Persons 7 Years of Age and Older

History of Adsorbed Tetanus Toxoid (Doses)	Clean, Minor Wounds		All Other Wounds*	
	Td	TIG	Td	TIG
Unknown or <three	Yes	No	Yes	Yes
≥Three†	No‡	No	No§	No

* Such as, but not limited to, wounds contaminated with dirt, puncture wounds and traumatic wounds.
† If only three doses of fluid tetanus toxoid have been received, then a fourth dose of toxoid, preferably an adsorbed toxoid should be given.
‡ Yes, if >10 years since last dose.
§ Yes, if >5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)

2.5 Administration

Just before use, shake the vial or syringe 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 these conditions exist, the product should not be administered.

When withdrawing a dose from a rubber-stoppered vial, do not remove either the rubber stopper or the metal seal holding it in place.

Each 0.5 mL dose of TENIVAC vaccine is to be administered intramuscularly. The preferred site is the deltoid muscle. 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.

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

3 DOSAGE FORMS AND STRENGTHS

TENIVAC vaccine is a suspension for injection available in 0.5 mL single-dose vials or syringes. [See *Description (11).*]

4 CONTRAINDICATIONS

4.1 Hypersensitivity

A severe allergic reaction (e.g., anaphylaxis) after a previous dose of TENIVAC vaccine or any other tetanus toxoid or diphtheria toxoid-containing vaccine or any other component of this vaccine is a contraindication to administration of TENIVAC vaccine. [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.

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

The tip caps of the TENIVAC prefilled syringes may contain natural rubber latex, which may cause allergic reactions in latex sensitive individuals.

5.3 Frequency of Administration

More frequent doses of TENIVAC vaccine than described in Section 2, Dosage and Administration, may be associated with increased incidence and severity of adverse reactions. [See *Dosage and Administration (2.1, 2.2, 2.3, 2.4)*.]

5.4 Arthus Reactions

Persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine usually have high serum tetanus antitoxin levels and should not receive TENIVAC vaccine more frequently than every 10 years, even for tetanus prophylaxis as part of wound management.

5.5 Guillain-Barré Syndrome and Brachial Neuritis

A review by the Institute of Medicine found evidence for a causal relation between tetanus toxoid and both brachial neuritis and Guillian-Barré syndrome. (2) If Guillain-Barré syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give TENIVAC vaccine or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.

5.6 Limitations of Vaccine Effectiveness

Vaccination with TENIVAC vaccine may not protect all individuals.

5.7 Altered Immunocompetence

If TENIVAC vaccine is administered to immunocompromised persons, including persons receiving immunosuppressive therapy, the expected immune response may not be obtained. [See *Drug Interactions (7.3)*.]

6 ADVERSE REACTIONS

6.1 Data from Clinical Studies

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 primary immunization study conducted in Canada, 18 participants, 8 of whom were 6 to 9 years of age and 10 of whom were 17 to 56 years of age, received three doses of TENIVAC vaccine. In four booster immunization studies conducted in either the US or Canada, TENIVAC vaccine was administered to 3,723 participants overall, ranging in age from 11 to 93 years.

In one of these studies, a US multi-center booster immunization study (TDC01), 2,250 adolescents and adults ages 11-59 years of age received TENIVAC vaccine in an open-label design and adults 60 years of age and over were randomized to receive either TENIVAC vaccine (N = 700) or DECAVAC vaccine (US licensed Td manufactured by Sanofi Pasteur Inc.) (N = 701). Vaccine assignment for participants ≥60 years of age was unblinded to pharmacists and vaccination nurses, but was blinded to other study personnel and participants. Among participants who received TENIVAC vaccine, overall, 80.4% were Caucasian, 3.3% Black, 5.1% Hispanic, 4.5% Asian and 6.6% other races. Among participants ≥60 years of age, the racial distribution was similar for the TENIVAC vaccine and DECAVAC vaccine groups. Among participants who received TENIVAC vaccine, the proportion of participants who were female varied by age group (44.4% of participants 11-18 years of age, 70.1% of participants 19-59 years of age and 62.4% of participants ≥60 years of age). Among participants ≥60 years of age who received DECAVAC vaccine, 57.6% were female. Nearly all (99.8%) enrolled participants and all participants in the per-protocol immunogenicity population had a reported or documented history of previous immunization against tetanus and diphtheria and, by report, had not received a vaccine containing tetanus or diphtheria toxoid within 5 years prior to enrollment.

In the US multi-center booster immunization study, solicited injection site reactions and systemic adverse events were monitored on diary cards for a subset of participants 11-59 years of age and for all participants ≥60 years of age. The incidence and severity of solicited injection site reactions and selected solicited systemic adverse events that occurred within 3 days following vaccination are shown in Table 2.

Table 2: Frequency and Severity of Selected Solicited Adverse Events Within 0-3 Days Following TENIVAC Vaccine or DECAVAC Vaccine in a US Study

	TENIVAC Vaccine			**DECAVAC Vaccine**
	Adolescents 11 to 18 years N = 491-492 %	**Adults 19 to 59 years N = 247 %**	**Adults ≥60 years N = 688-695 %**	**Adults ≥60 years N = 686-693 %**
Injection Site Adverse Reactions				
Pain				
Any	80.1	74.9	35.3	29.4
Moderate*	15.0	18.2	2.9	2.3
Severe†	0.2	0.4	0.6	0.7
Redness				
Any	25.6	15.8	18.1	18.0
≥35 mm to <50 mm	1.2	2.4	0.7	1.3
≥50 mm	0.4	0.4	2.3	1.9
Swelling				
Any	15.0	17.0	12.1	13.0
≥35 mm to <50 mm	1.2	2.8	1.0	1.3
≥50 mm	1.8	2.8	1.7	1.3
Systemic Adverse Events				
Fever				
≥37.5°C	4.3	5.7	2.5	3.8
≥38.0°C to <39°C	0.8	1.6	0.6	0.9
≥39°C	0.0	0.0	0.1	0.1
Headache				

	TENIVAC Vaccine			**DECAVAC Vaccine**
	Adolescents 11 to 18 years N = 491-492 %	**Adults 19 to 59 years N = 247 %**	**Adults ≥60 years N = 688-695 %**	**Adults ≥60 years N = 686-693 %**
Any	23.0	25.1	11.7	10.8
Moderate*	4.3	7.3	1.6	1.4
Severe†	0.6	0.8	0.0	0.3
Muscle Weakness				
Any	32.3	17.4	4.9	5.9
Moderate*	7.3	3.2	1.3	1.0
Severe†	0.6	0.4	0.1	0.1
Malaise				
Any	14.5	17.0	8.9	8.8
Moderate*	3.5	3.2	2.4	1.2
Severe†	0.8	0.4	0.1	0.4
Pain in Joints				
Any	15.7	10.9	8.5	7.4
Moderate*	2.8	1.6	2.2	1.4
Severe†	0.6	0.4	0.1	0.0

* Moderate: interfered with activities, but did not require medical care or absenteeism.

† Severe: incapacitating, unable to perform usual activities, may have/or required medical care or absenteeism.

In the US booster immunization study, among participants ≥60 years of age, 7 (1.0%) participants in the TENIVAC vaccine group and 10 (1.4%) participants in the DECAVAC vaccine group experienced a serious adverse event within 30 days following vaccination. During this period, 2 (0.3%) participants 19-59 years of age and no participants 11-18 years of age experienced a serious adverse event following TENIVAC vaccine. Serious adverse events within 30 days following TENIVAC vaccine included localized infection, asthma, colonic polyp, cellulitis, angina pectoris, hip and wrist fracture, cholecystitis, chest pain and cerebrovascular accident.

There were five deaths reported during the study. All of the reported deaths were in participants ≥60 years of age and occurred >30 days post-vaccination: three in the TENIVAC vaccine group (cardiopulmonary arrest; myocardial infarction and septic shock; and unknown cause) and two in the DECAVAC vaccine group (myocardial infarction and congestive heart failure; and liver cancer).

In the primary immunization study (N = 18) in which serious adverse events were monitored for 3 days following each vaccination and in three other booster immunization studies in which serious adverse events were monitored for either four days (N = 347) or one month (N = 426) following vaccination, no serious adverse events were reported.

6.2 Data from Post-marketing Experience

The following adverse events have been spontaneously reported during the post-marketing use of TENIVAC vaccine. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

The following adverse events were included based on severity, frequency of reporting or the strength of causal association to TENIVAC vaccine:

- **Blood and lymphatic system disorders**

Lymphadenopathy

- **Immune system disorders**

Allergic reactions (such as erythematous rash, maculopapular rash, urticaria and pruritus); anaphylactic reaction (bronchospasm and angioedema).

- **Nervous system disorders**

Paresthesia, dizziness, syncope

Guillain Barré syndrome

- **Gastrointestinal disorders**

Vomiting

- **Musculoskeletal, connective tissue and bone disorders**

Myalgia, pain in extremities

- **General disorders and administration site conditions**

Injection site reactions (including inflammation, mass, edema, induration, warmth, pruritus, cellulitis, discomfort)

Fatigue, edema peripheral

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration

No safety and immunogenicity data are available on the concomitant administration of TENIVAC vaccine with other US licensed vaccines.

7.2 Tetanus Immune Globulin (Human)

If passive protection against tetanus is required, TIG (Human) may be administered according to its prescribing information, concomitantly with TENIVAC vaccine at a separate site with a separate needle and syringe. [See *Dosage and Administration (2.4).*]

7.3 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 TENIVAC vaccine. [See *Warnings and Precautions (5.7).*]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with TENIVAC vaccine. It is also not known whether TENIVAC vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. TENIVAC vaccine should be given to a pregnant woman only if clearly needed.

Animal fertility studies have not been conducted with TENIVAC vaccine. The effect of TENIVAC vaccine on embryo-fetal and pre-weaning development was evaluated in one developmental toxicity study using pregnant rabbits. Animals were administered TENIVAC vaccine twice prior to gestation, during the period of organogenesis (gestation day 6) and later during pregnancy on gestation day 29, 0.5 mL/rabbit/occasion (a 17-fold increase compared to the human dose of TENIVAC vaccine on a body weight basis), by intramuscular injection. No adverse effects on pregnancy, parturition, lactation, embryo-fetal or pre-weaning development were observed. There were no vaccine related fetal malformations or other evidence of teratogenesis noted in this study.

8.3 Nursing Mothers

It is not known whether TENIVAC vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TENIVAC vaccine is administered to a nursing woman.

8.4 Pediatric Use

TENIVAC vaccine is not approved for use in infants and children younger than 7 years of age. Safety and effectiveness of TENIVAC vaccine in this age group have not been established.

8.5 Geriatric Use

In one clinical study, (TDC01) 449 participants 65 years of age and over, including 192 participants who were 75 years of age and over received a dose of TENIVAC vaccine. A lower proportion of participants 65 years of age and over had a pre-vaccination seroprotective level of antibody to tetanus toxoid and diphtheria toxin compared to adolescents and adults less than 65 years of age. The proportion of participants 65 years of age and over with a seroprotective level of antibody following TENIVAC vaccine was marginally lower for tetanus and lower for diphtheria compared to younger participants. In general, rates of solicited adverse events were not higher in participants 65 years of age and over compared to younger participants. [See *Adverse Reactions (6), Clinical Pharmacology (12.1),* and *Clinical Studies (14.2)*.]

11 DESCRIPTION

TENIVAC vaccine, Tetanus and Diphtheria Toxoids Adsorbed, is a sterile isotonic suspension of tetanus and diphtheria toxoids adsorbed on aluminum phosphate.

Each 0.5 mL dose of TENIVAC vaccine contains the following active ingredients:

Tetanus Toxoid 5 Lf

Diphtheria Toxoid 2 Lf

Other ingredients per 0.5 mL dose include 1.5 mg of aluminum phosphate (0.33 mg of aluminum) as the adjuvant and ≤5.0 mcg of residual formaldehyde.

Clostridium tetani is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (3) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulfate fractionation and diafiltration. *Corynebacterium diphtheriae* is grown in modified Mueller's growth medium. (4) After purification by ammonium sulfate fractionation, diphtheria toxin is detoxified with formaldehyde and diafiltered. Tetanus and diphtheria toxoids are individually adsorbed onto aluminum phosphate.

The adsorbed tetanus and diphtheria toxoids are combined with aluminum phosphate (as adjuvant), sodium chloride and water for injection. This product contains no preservative.

In the guinea pig potency test, the tetanus toxoid component induces at least 2 neutralizing units/mL of serum and the diphtheria toxoid component induces at least 0.5 neutralizing units/mL of serum.

The tip caps of the prefilled syringes may contain natural rubber latex. The vial stoppers do not contain latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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

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. (5) A level of at least of 1.0 IU/mL has been associated with long-term protection. (7)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

14 CLINICAL STUDIES

14.1 Primary Immunization

A three-dose primary immunization series with TENIVAC vaccine was evaluated in 17 participants ages 6 to 56 years in a study conducted in Canada. [See *Adverse Reactions (6.1)*.] The

first two doses were administered two months apart, followed by a third dose six to eight months after the second dose. Serum tetanus antitoxin levels were measured by an *in vivo* neutralizing assay and serum diphtheria antitoxin levels were measured by an *in vitro* neutralizing assay. [See *Clinical Pharmacology (12.1)*.] All 17 participants had serum tetanus and diphtheria antitoxin levels pre-vaccination and 7 days post-vaccination <0.01 IU/mL, consistent with no previous immunization. Four weeks following the second dose, all 17 participants had a serum tetanus antitoxin level >0.1 IU/mL and a serum diphtheria antitoxin level ≥0.01 IU/mL. Four weeks following the third dose, all 17 participants had a serum diphtheria antitoxin level >0.1 IU/mL.

14.2 Booster Immunization

In the US multicenter booster immunization study (TDC01) [see *Adverse Reactions (6.1)*], the immune response to a dose of TENIVAC vaccine was evaluated in an open-label manner in a subset of participants 11 to 59 years of age, and in comparison to DECAVAC vaccine in participants ≥60 years of age who were randomized to receive a dose of either TENIVAC vaccine or DECAVAC vaccine. Tetanus immune responses, measured by ELISA [see *Clinical Pharmacology (12.1)*] are presented in Table 3. Diphtheria immune responses, measured by a microneutralization assay [see *Clinical Pharmacology (12.1)*], are presented in Table 4.

Among adults 65 years of age and over who received TENIVAC vaccine (N = 419), 94.5% (95% confidence interval 91.9, 96.5) had a post-vaccination tetanus antitoxoid level ≥0.1 IU/mL and 61.1% (95% confidence interval 56.2, 65.8) had a post-vaccination diphtheria antitoxoid level ≥0.1 IU/mL.

277 **Table 3: Tetanus Antitoxoid Levels and Booster Response Rates Following a Dose of**

278 **TENIVAC Vaccine, by Age Group, and for Adults ≥60 Years of Age, Compared to**

279 **DECAVAC Vaccine, per Protocol Immunogenicity Population**

Treatment Group	Age Group	Timing	Percent of Participants With Specified Level of Tetanus Antitoxoid and Booster Response		
			≥0.1 IU/mL % (95% CI)	≥1.0 IU/mL % (95% CI)	Booster Response* % (95% CI)
TENIVAC vaccine	Adolescents 11 to 18 years (N = 470)	Pre-	97.9 (96.1, 99.0)	48.7 (44.1, 53.3)	-
		Post-	100.0 (99.2, 100)	99.8 (98.8, 100)	92.8 (90.0, 94.9)
	Adults 19 to 59 years (N = 237)	Pre-	97.5 (94.6, 99.1)	77.6 (71.8, 82.8)	-
		Post-	100.0 (98.5, 100)	99.6 (97.7, 100)	84.0 (78.7, 88.4)
	Adults ≥60 years (N = 661)	Pre-	76.2 (72.8, 79.4)	43.7 (39.9, 47.6)	-
		Post-	96.1† (94.3, 97.4)	90.6‡ (88.1, 92.7)	82.3§ (79.2, 85.1)
DECAVAC vaccine	Adults ≥60 years (N = 658)	Pre-	75.2 (71.7, 78.5)	45.7 (41.9, 49.6)	-
		Post-	97.3 (95.7, 98.4)	91.9 (89.6, 93.9)	83.7 (80.7, 86.5)

* Booster response: If pre-vaccination level ≤0.10 IU/mL, 4-fold increase and post-vaccination level ≥0.10 IU/mL. If pre-vaccination level >0.10 IU/mL and ≤2.7 IU/mL, 4-fold increase. If pre-vaccination level >2.7 IU/mL, 2-fold increase.

† TENIVAC vaccine non-inferior to DECAVAC vaccine [upper limit of 95% CI for difference (DECAVAC vaccine minus TENIVAC vaccine) <5%].

‡ Non-inferiority criteria not prospectively specified for this endpoint.

§ TENIVAC vaccine non-inferior to DECAVAC vaccine [upper limit of 95% CI for difference (DECAVAC vaccine minus TENIVAC vaccine) <10%].

Pre- indicates pre-vaccination bleed.

Post- indicates 26-42 days post-vaccination bleed.

Table 4: Diphtheria Antitoxin Levels and Booster Response Rates Following a Dose of TENIVAC Vaccine, by Age Group, and for Adults ≥60 Years of Age, Compared to DECAVAC Vaccine, per Protocol Immunogenicity Population

Treatment Group	Age Group	Timing	Percent of Participants With Specified Level of Diphtheria Antitoxin and Booster Response			
			≥0.01 IU/mL % (95% CI)	≥0.1 IU/mL % (95% CI)	≥1.0 IU/mL % (95% CI)	Booster Response* % (95% CI)
TENIVAC vaccine	Adolescents 11 to 18 years (N = 470)	Pre-	99.1 (97.8, 99.8)	78.7 (74.7, 82.3)	18.5 (15.1, 22.3)	-
		Post-	100.0 (99.2, 100)	99.8 (98.8, 100)	98.9 (97.5, 99.7)	95.7 (93.5, 97.4)
	Adults 19 to 59 years (N = 237)	Pre-	96.6 (93.5, 98.5)	73.0 (66.9, 78.5)	18.6 (13.8, 24.1)	-
		Post-	99.2 (97.0, 99.9)	97.5 (94.6, 99.1)	91.1 (86.8, 94.4)	89.9 (85.3, 93.4)
	Adults ≥60 years (N = 661)	Pre-	61.9 (58.1, 65.6)	29.0 (25.6, 32.7)	8.5 (6.5, 10.9)	-
		Post-	88.0† (85.3, 90.4)	71.1‡ (67.5, 74.5)	47.5† (43.6, 51.4)	65.5‡ (61.7, 69.1)
DECAVAC vaccine	Adults ≥60 years (N = 658)	Pre-	61.7 (57.9, 65.4)	32.2 (28.7, 35.9)	10.5 (8.3, 13.1)	-
		Post-	87.4 (84.6, 89.8)	70.7 (67.0, 74.1)	45.7 (41.9, 49.6)	62.9 (59.1, 66.6)

* Booster response: If pre-vaccination level ≤0.10 IU/mL, 4-fold increase and post-vaccination level ≥0.10 IU/mL. If pre-vaccination level >0.10 IU/mL and ≤2.56 IU/mL, 4-fold increase. If pre-vaccination level >2.56 IU/mL, 2-fold increase.

† Non-inferiority criteria not prospectively specified for this endpoint.

‡ TENIVAC vaccine non-inferior to DECAVAC vaccine [upper limit of 95% CI for difference (DECAVAC vaccine minus TENIVAC vaccine) <10%].

Pre- indicates pre-vaccination bleed.

Post- indicates 26-42 days post-vaccination bleed.

15 REFERENCES

1 CDC. Diphtheria, tetanus and pertussis: recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991;40(RR-10):1-28.

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4 Stainer DW. Production of diphtheria toxin. In: Manclark CR, editor. Proceedings of an informal consultation on the World Health Organization requirements for diphtheria, tetanus, pertussis and combined vaccines. United States Public Health Services, Bethesda, MD. DHHS 91-1174. 1991. p. 7-11.

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.

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7 Vitek CR and Wharton M. Diphtheria toxoid. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 5th ed. Philadelphia, PA: W.B. Saunders Company; 2008. p. 139-56.

16 HOW SUPPLIED/STORAGE AND HANDLING

Vial, 1 dose - NDC No. 49281-215-58; in package of 10 vials, NDC No. 49281-215-10. Contains no latex.

Syringe, 1 dose– NDC No. 49281-215-88; in package of 10 syringes, NDC No. 49281-215-15. The tip caps of the prefilled syringes may contain natural rubber latex. No other components contain latex.

TENIVAC vaccine 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 TENIVAC vaccine health-care providers should inform the patient, parent or guardian of the benefits and risks of the vaccine and the importance of completing the primary immunization series or receiving recommended booster doses, as appropriate, unless a contraindication to further immunization exists.

The health-care provider should inform the patient, parent or guardian about the potential for adverse reactions that have been temporally associated with TENIVAC vaccine or other vaccines containing similar components. The health-care provider should provide the Vaccine Information Statements (VISs) which are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization. Patients, parents, or guardians should be instructed to report adverse reactions to their health-care provider.

Product information as of April 2013.

Manufactured by:

Sanofi Pasteur Limited

Toronto Ontario Canada

Distributed by:

Sanofi Pasteur Inc.

Swiftwater PA 18370 USA

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