Diphtheria and Tetanus Toxoids Adsorbed is a vaccine indicated for active immunization against diphtheria and tetanus. Diphtheria and Tetanus Toxoids Adsorbed is approved for use in children from 6 weeks through 6 years of age (prior to 7th birthday). (1)

**INDICATIONS AND USAGE**

Diphtheria and Tetanus Toxoids Adsorbed is a vaccine indicated for active immunization against diphtheria and tetanus. Diphtheria and Tetanus Toxoids Adsorbed is approved for use in children from 6 weeks through 6 years of age (prior to 7th birthday). (1)

**DOSE AND ADMINISTRATION**

The five dose immunization series consists of an injection administered at 2, 4, 6, 15-18 months and between 4 and 6 years of age. (2.1)

**DOSE FORMS AND STRENGTHS**

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

**CONTRAINDICATIONS**

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of Diphtheria and Tetanus Toxoids Adsorbed or any other diphtheria toxoid or tetanus toxoid-containing vaccine, or any other component of this vaccine. (4)

**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 CLINICAL PHARMACOLOGY
10 DESCRIPTION
11 REFERENCES
12 HOW SUPPLIED/STORAGE AND HANDLING
13 PATIENT COUNSELING INFORMATION

**WARNINGS AND PRECAUTIONS**

- 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 Diphtheria and Tetanus Toxoids Adsorbed vaccine. (5.2)
- Anaphylaxis following intramuscular vaccination has been observed in some infants born premature. The decision about when to administer an intramuscular vaccine, including Diphtheria and Tetanus Toxoids Adsorbed, to an infant born prematurely should be based on consideration of the individual infant's medical status and the potential benefits and possible risks of vaccination. (5.5)
- Syncope (fainting) has been reported following vaccination with Diphtheria and Tetanus Toxoids Adsorbed vaccine. Procedures should be in place to prevent falling injury and manage syncopal reactions. (5.6)

**ADVERSE REACTIONS**

The most common adverse reactions (≥5%) were crying, fever, and loss of appetite. (6.1)

**DRUG INTERACTIONS**

Immunosuppressive therapies may reduce the response to Diphtheria and Tetanus Toxoids Adsorbed. (7.3)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 03/2019
6 ADVERSE REACTIONS

The most common adverse reactions (≥5%) were crying, fever, and loss of appetite.

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 clinical trial in Baltimore, 163 infants received Diphtheria and Tetanus Toxoids Adsorted at 2, 4, and 6 months of age. The results of this trial are presented in Table 1.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Dose 1 (% (n = 163)</th>
<th>Dose 2 (% (n = 145)</th>
<th>Dose 3 (% (n = 136)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever ≥38°C &lt;39°C (≥100.4°F &lt;102.2°F)</td>
<td>0.7</td>
<td>0.8</td>
<td>6.6</td>
</tr>
<tr>
<td>Fever ≥39°C (≥102.2°F)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Crying</td>
<td>13.6</td>
<td>15.2</td>
<td>13.0</td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>3.9</td>
<td>6.2</td>
<td>2.9</td>
</tr>
</tbody>
</table>

Table 1: Percentage of Children Experiencing Local and Systemic Reactions at 24 Hours Following Immunization

6.2 Lactation

Diphtheria and Tetanus Toxoids Adsorted is not approved for use in individuals 7 years of age and older. Human or animal data are not available to assess vaccine-associated risks in pregnancy.

7 DRUG INTERACTIONS

7.1 Concomitant Administration with Other Vaccines

No safety and immunogenicity data are available on the concomitant administration of Diphtheria and Tetanus Toxoids Adsorted with other US licensed vaccines.

7.2 Concomitant Administration with Tetanus Immune Globulin (Human)

If passive protection against tetanus is required, TIG (Human) may be administered according to its prescribing information, concomitantly with Diphtheria and Tetanus Toxoids Adsorted at a separate site with a separate needle and syringe.

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 Diphtheria and Tetanus Toxoids Adsorted. [See Warnings and Precautions (5.4).]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Diphtheria and Tetanus Toxoids Adsorted is not approved for use in individuals 7 years of age and older. Human or animal data are not available to assess the impact of Diphtheria and Tetanus Toxoids Adsorted on milk production, its presence in breast milk, or its effects on the breastfed infant.

8.2 Lactation

Diphtheria and Tetanus Toxoids Adsorted is not approved for use in individuals 7 years of age and older. Human or animal data are not available to assess the impact of Diphtheria and Tetanus Toxoids Adsorted on milk production, its presence in breast milk, or its effects on the breastfed infant.

8.4 Pediatric Use

Diphtheria and Tetanus Toxoids Adsorted is not indicated for infants below 6 weeks of age or children 7 years of age or older. Safety and effectiveness of Diphtheria and Tetanus Toxoids Adsorted in these age groups have not been established.

9 DESCRIPTION

Diphtheria and Tetanus Toxoids Adsorted is a sterile, cloudy, white, uniform suspension of diphtheria and tetanus toxoids adsorbed on aluminum phosphate and suspended in isotonic sodium chloride solution for intramuscular injection only. Diphtheria and Tetanus Toxoids Adsorted vaccine does not contain a preservative.

Each 0.5 mL dose is formulated to contain: 25 Lf diphtheria toxoid and 5 Lf tetanus toxoid. Other ingredients per 0.5 mL dose include: 1.5 mg aluminum phosphate and <100 mcg free formaldehyde. Diphtheria toxoid is prepared from the toxin produced during the growth of a selected strain of Corynebacterium diphtheriae grown with aeration in submerged culture. The toxin is purified by precipitation, converted to toxoid by the addition of formalin and concentrated by precipitation. The culture medium consists of a tyrpic digest of casein, supplemented with cystine, malate, uracil, inorganic salts and vitamins.

Tetanus toxoid is prepared from the toxin produced during the growth of a selected strain of Clostridium tetani. The toxin is converted to toxoid by the addition of formalin, concentrated and then purified. The culture medium consists of a tyrpic digest of casein, supplemented with cystine, dextrose, uracil, inorganic salts and vitamins. When tested in guinea pigs, the tetanus and diphtheria components induce at least 2 neutralizing units/mL of serum.

The vial stopper is not made with natural rubber latex.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

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 0.1 International Units (IU)/mL is the lowest level giving some degree of protection, and levels of at least 0.1 IU/mL are generally regarded as protective. (3) (4) 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 0.1 IU/mL, measured by neutralization assay is considered the minimum protective level. (3) (5)

11 NONCLINICAL TOXICOLOGY

11.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Diphtheria and Tetanus Toxoids Adsorted has not been evaluated for carcinogenicity, mutagenic potential, or impairment of fertility.

11.2 Clinical Studies

In a clinical study conducted in Baltimore, MD, infants received one of three lots of Diphtheria and Tetanus Toxoids Adsorted (formulation that contained thimerosal), 0.5 mL, at 2, 4 and 6 months of age. Oral poliovirus vaccine (no longer licensed in the US) was administered concomitantly with Diphtheria and Tetanus Toxoids Adsorted concurrently at a separate site with Diphtheria and Tetanus Toxoids Adsorted at 2 and 4 months of age. Diphtheria and tetanus antitoxin levels were evaluated at 8 months of age (see Table 2). Protective levels of diphtheria antitoxin (≥0.01 IU/mL) and tetanus antitoxin (≥0.01 IU/mL) were detected in 99% and 100%, respectively, of the Diphtheria and Tetanus Toxoids Adsorted recipients after 3 doses. The geometric mean titers (GMT) for diphtheria and tetanus antitoxin antibodies in recipients of the three Diphtheria and Tetanus Toxoids Adsorted lots were not significantly different, ranging from 0.25 to 0.35 IU/mL for diphtheria antitoxin antibodies, and from 0.75 to 0.80 IU/mL for tetanus antibodies after the third dose. In a group of 75 infants who received an investigational acellular pertussis vaccine simultaneously with the Diphtheria and Tetanus Toxoids Adsorted but at separate sites with separate needles and syringes, protective diphtheria and tetanus antitoxin levels developed in 100% of the recipients.

Table 2: Percentage of Children Protected Following Administration of Diphtheria and Tetanus Toxoids Adsorted

<table>
<thead>
<tr>
<th>Post Dose 3 Diphtheria and Tetanus Toxoids Adsorted</th>
<th>Diphtheria antitoxin ≥0.01 IU/mL</th>
<th>99% (135/136)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tetanus antitoxin ≥0.01 IU/mL</td>
<td>100% (137/137)</td>
</tr>
</tbody>
</table>

12 REFERENCES

16  HOW SUPPLIED/STORAGE AND HANDLING

Diphtheria and Tetanus Toxoids Adsorbed is supplied in:
- a 0.5 mL single-dose vial: NDC No. 49281-225-58;
- in packages of 10 vials: NDC No. 49281-225-10.

The vial stopper is not made with natural rubber latex.

Diphtheria and Tetanus Toxoids Adsorbed 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 vaccine beyond the expiration date. Discard unused portion.

17  PATIENT COUNSELING INFORMATION

Inform the parent or guardian of the following:
- It is important to complete the immunization series for maximum protection against diphtheria and tetanus.
- Common adverse reactions include local redness, swelling, and tenderness at the injection site, fever, crying, and loss of appetite.
- Other adverse reactions can occur. Call your 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
R7-0319 USA

DTA-FPLR-SL-MAR19 Rx Only