093 90426-0

A.H.F.S. Category 80:12

Typhoid Vi Polysaccharide Vaccine Typhim Vi®

℞ only

Caution: Federal (USA) law prohibits dispensing without prescription.

DESCRIPTION

Typhim Vi®, Typhoid Vi Polysaccharide Vaccine, produced by Aventis Pasteur SA, for intramuscular use, is a sterile solution containing the cell surface Vi polysaccharide extracted from *Salmonella typhi* Ty2 strain. The organism is grown in a semi-synthetic medium without animal proteins. The capsular polysaccharide is precipitated from the concentrated culture supernatant by the addition of hexadecyltrimethylammonium bromide and the product is purified by differential centrifugation and precipitation. The potency of the purified polysaccharide is assessed by molecular size and O-acetyl content. Phenol, 0.25%, is added as a preservative. The vaccine contains residual polydimethylsiloxane or fatty-acid ester-based antifoam. The vaccine is a clear, colorless solution. Each single-dose of 0.5 mL is formulated to contain 25 µg of purified Vi polysaccharide in a colorless isotonic phosphate buffered saline (pH 7 ± 0.3), 4.150 mg of Sodium Chloride, 0.065 mg of Disodium Phosphate ($2H_20$), 0.023 mg of Monosodium Phosphate and 0.5 mL of Sterile Water for Injection.

CLINICAL PHARMACOLOGY

Typhoid fever is an infectious disease caused by *S. typhi*. Humans are the only natural host and reservoir for *S. typhi*; infections result from the consumption of food or water that has been contaminated by the excretions of an acute case or a carrier. *S. typhi* organisms efficiently invade the human intestinal mucosae ultimately leading to bacteremia; following a typical 10- to 14-day incubation period, a systemic illness occurs. The clinical presentation of typhoid fever exhibits a broad range of severity and can be debilitating. Classical cases have fever, myalgia, anorexia, abdominal discomfort and headaches; the fever increases step-wise over a period of days and then may remain at 102°F to 106°F over 10 to 14 days before decreasing in a step-wise manner. Skin lesions known as rose spots may be present. Constipation is common in older children and adults, while diarrhea may occur in younger children. Among the less common but most severe complications are intestinal perforation and hemorrhage, and death. The course is typically more severe without appropriate antimicrobial therapy. The case fatality rate was reported to be approximately 10% to 20% in the pre-antibiotic era.[1,2,3] During the period of 1983 to 1991 in the US, the case fatality rate reported to the Centers for Disease Control and Prevention (CDC) was 0.2% (9/4010).[4] Infection of the gallbladder can lead to the chronic carrier state.

Typhoid fever is still endemic in many countries of the world where it is predominantly a disease of school-age children and may be a major public health problem. Most cases of typhoid fever in the US are thought to be acquired during foreign travel. During the periods of 1975 to 1984 and 1983 to 1984, respectively, 62% and 70% of the cases of typhoid fever reported to the CDC were acquired during foreign travel; this compares to 33% of cases during 1967-1972.[5]

In 1992, 414 cases of typhoid fever were reported to the CDC. Of these 414 cases, 1 (0.2%) case occurred in an infant under one year of age; 77 (18.6%) cases occurred in persons one to nine years of age; 81 (19.6%) cases occurred in persons 10 to 19 years of age; 251 (60.6%) cases occurred in individuals ≥ 20 years of age; the age was not available for 4 (1%) cases. One death was reported in 1991.[4] Domestic surveillance could underestimate the risk of typhoid fever in travelers since the disease is unlikely to be reported for persons who received diagnosis and treatment overseas.[6]

Approximately 2% to 4% of acute typhoid fever cases develop into a chronic carrier state. The chronic carrier state occurs more frequently with advanced age, and among females than males.[2,7] These non-symptomatic carriers are the natural reservoir for *S. typhi* and can serve to maintain the disease in its endemic state or to directly infect new individuals. Outbreaks of typhoid fever are often traced to food handlers who are asymptomatic carriers.[8]

Other vaccines used for the prevention of typhoid fever in selected populations include a parenteral vaccine containing killed *S. typhi* bacteria and an oral vaccine with live, attenuated *S. typhi*. Typhim Vi, consisting of purified *S. typhi* Vi capsular polysaccharide, is a different type of vaccine.

Two formulations were utilized in studies of the typhoid Vi polysaccharide vaccine. These included the liquid formulation which is identical to Typhim Vi and a lyophilized formulation.

The protective efficacy of each of these formulations of the typhoid Vi polysaccharide vaccine was assessed independently in two trials conducted in areas where typhoid fever is endemic. A single intramuscular dose of 25 µg was used in these efficacy studies. A randomized double-blind controlled trial with Typhim Vi (liquid formulation) was conducted in five villages west of Katmandu, Nepal. There were 6,908 vaccinated subjects: 3,454 received Typhim Vi and 3,454 in the control group received a 23-valent pneumococcal polysaccharide vaccine. Of the 6,908 subjects, 6,439 subjects were in the target population of 5 to 44 years of age. In addition, 165 children ages 2 to 4 years and 304 adults over 44 years of age were included in the study. The overall protective efficacy of Typhim Vi was 74% (95% confidence interval (CI): 49% to 87%) for blood culture confirmed cases of typhoid fever during 20 months of post-vaccination follow-up.[9,10,11]

The protective efficacy of the typhoid Vi polysaccharide vaccine, lyophilized formulation, was evaluated in a randomized double-blind controlled trial conducted in South Africa. There were 11,384 vaccinated children 5 to 15 years of age; 5,692 children received the Vi capsular polysaccharide vaccine and 5,692 in the control group received meningococcal polysaccharide (Groups A+C) vaccine. The protective efficacy for the Vi capsular polysaccharide (lyophilized formulation) group for blood culture confirmed cases of typhoid fever was 55% (95% CI: 30% to 70%) overall during 3 years of post-vaccination follow-up, and was 61%, 52% and 50%, respectively, for years 1, 2, and 3. Vaccination was associated with an increase in anti-Vi antibodies as measured by radioimmunoassay (RIA) and enzyme-linked immunosorbent assay. Antibody levels remained elevated at 6 and 12 months post-vaccination.[11,12]

Because of the very low incidence of typhoid fever in the US, efficacy studies are not currently feasible in this population.

Controlled comparative efficacy studies of Typhim Vi and other types of typhoid vaccines have not been performed.

An increase in serum anti-capsular antibodies is thought to be the basis of protection provided by Typhim Vi. However, a specific correlation of post-vaccination antibody levels with subsequent protection is not available and the level of Vi antibody that will provide protection has not been determined. Also, limitations exist for comparing immunogenicity results from subjects in endemic areas, where some subjects have baseline serological evidence of prior *S. typhi* exposure, to naive populations such as most American travelers.

In endemic regions (Nepal, South Africa, Indonesia) where trials were conducted, pre-vaccination geometric mean antibody levels suggest that infection with *S. typhi* has previously occurred in a large percentage of the vaccinees. In these populations, specific antibody levels increased four-fold or greater in 68% to 87.5% of older children and adult subjects following vaccination. For 43 persons 15 to 44 years of age in the Nepal pilot study, geometric mean specific antibody levels pre- and 3 weeks post-vaccination were, respectively, 0.38 and 3.68 µg antibody/mL by RIA; 79% had a four-fold or greater rise in Vi antibody levels.[9,12]

Immunogenicity and safety trials were conducted in a racially mixed US population. A single dose of Typhim Vi vaccine induced a four-fold or greater increase in antibody levels in 88% and 96% of this adult population for 2 studies, respectively, following vaccination (see TABLE 1).[10,13]

TABLE 1.[10,13] **Vi ANTIBODY LEVELS IN US ADULTS 18 TO 40 YEARS OF AGE GIVEN TYPHIM Vi**

		GEOMETRIC MEAN ANTIBODY LEVELS (µg antibody/mL by RIA)		
	N	**Pre** **(95% CI)**	**Post (4 weeks)**	**% ≥4 FOLD INCREASE (95% CI)**
Trial 1 (1 lot)	54	0.16 (0.13 to 0.21)	3.23 (2.59 to 4.03)	96% (52/54) (87% to 100%)
Trial 2 (2 lots combined)	97	0.17 (0.14 to 0.21)	2.86 (2.26 to 3.62)	88% (85/97) (81% to 94%)

No studies of safety and immunogenicity have been conducted in US children. A double-blind randomized controlled trial testing the safety and immunogenicity of Typhim Vi was performed in 175 Indonesian children. The percentage of 2- to 5-year-old children achieving a four-fold or greater increase in antibody levels at 4 weeks post-vaccination was 96.3% (52/54) (95% CI: 87.3% to 99.6%), and in the study subset of 2-year-old children was 94.4% (17/18) (95% CI: 72.7% to 99.9%). The geometric mean levels (µg antibody/mL by RIA) for the 2-to 5-year-old children and the subset of 2-year-olds were, respectively, 5.81 (4.36 to 7.77) and 5.76 (3.48 to 9.53).[10,11]

In the US Reimmunization Study, adults previously immunized with Typhim Vi in other studies were reimmunized with a 25 µg dose at 27 or 34 months after the primary dose. Data on antibody response to primary immunization, decline following primary immunization, and response to reimmunization are presented in TABLE 2. Antibody levels attained following reimmunization at 27 or 34 months after the primary dose were similar to levels attained following the primary immunization.[10,13] This response is typical for a T-cell independent polysaccharide vaccine in that reimmunization does not elicit higher antibody levels than primary immunization. The safety of reimmunization was also evaluated in this study (see **ADVERSE REACTIONS** section).

TABLE 2.[10,13] **US STUDIES IN 18- TO 40-YEAR-OLD ADULTS: KINETICS AND PERSISTENCE OF Vi ANTIBODY* RESPONSE TO PRIMARY IMMUNIZATION WITH TYPHIM Vi, AND RESPONSE TO REIMMUNIZATION AT 27 OR 34 MONTHS**

	PRE-DOSE 1	**1 MONTH**	**11 MONTHS**	**18 MONTHS**	**27 MONTHS**	**34 MONTHS**	**1 MONTH POST-REIMMUNIZATION[e]**
GROUP 1[a]							
N	43	43	39	ND[c]	43	ND	43
Level*	0.19	3.01	1.97		1.07[d]		3.04
95% CI	(0.14-0.26)	(2.22-4.06)	(1.31-3.00)		(0.71-1.62)		(2.17-4.26)
GROUP 2[b]							
N	12	12	ND	10	ND	12	12
Level	0.14	3.78		1.21		0.76[d]	3.31
95% CI	(0.11-0.18)	(2.18-6.56)		(0.63-2.35)		(0.37-1.55)	(1.61-6.77)

* µg antibody/mL by RIA
[a] Group 1: Reimmunized at 27 months following primary immunization.
[b] Group 2: Reimmunized at 34 months following primary immunization.
[c] Not Done
[d] Antibody levels pre-reimmunization.
[e] Includes available data from all reimmunized subjects (subjects initially randomized to Typhim Vi, and subjects initially randomized to placebo who received open label Typhim Vi two weeks later).

INDICATIONS AND USAGE

Typhim Vi vaccine is indicated for active immunization against typhoid fever for persons two years of age or older.

Immunization with Typhim Vi should occur at least two weeks prior to expected exposure to *S. typhi*.

Routine immunization against typhoid fever is not recommended in the United States.[14]

Selective immunization against typhoid fever is recommended under the following circumstances: 1) travelers to areas where a recognized risk of exposure to typhoid exists, particularly ones who will have prolonged exposure to potentially contaminated food and water, 2) persons with intimate exposure (i.e., continued household contact) to a documented typhoid carrier, and 3) workers in microbiology laboratories who frequently work with *S. typhi*.[14]

Typhoid vaccination is not required for international travel, but is recommended for travelers to areas where there is a recognized risk of exposure to *S. typhi*. *S. typhi* is prevalent in many countries of Africa, Asia, and Central and South America. Current CDC advisories should be consulted with regard to specific locales. Vaccination is particularly recommended for travelers who will have prolonged exposure to potentially contaminated food and water. However, even travelers who have been vaccinated should use caution in selecting food and water.[15]

Based on the available efficacy data, vaccination with Typhim Vi may not be expected to protect 100% of susceptible individuals.

There is no evidence to support the use of typhoid vaccine to control common source outbreaks, disease following natural disaster or in persons attending rural summer camps.[16]

An optimal reimmunization schedule has not been established. Reimmunization every two years under conditions of repeated or continued exposure to the *S. typhi* organism is recommended at this time.

Typhim Vi has efficacy against typhoid fever caused by *S. typhi* infection but will not afford protection against species of *Salmonella* other than *S. typhi* or other bacteria that cause enteric disease.

For recommended primary immunization and reimmunization see **DOSAGE AND ADMINISTRATION** section.

Typhim Vi should not be used to treat a patient with typhoid fever or a chronic typhoid carrier.

CONTRAINDICATIONS

TYPHIM Vi IS CONTRAINDICATED IN PATIENTS WITH A HISTORY OF HYPERSENSITIVITY TO ANY COMPONENT OF THIS VACCINE.

WARNINGS

This product contains dry natural latex rubber as follows: The stopper to the vial contains no rubber of any kind. In the case of the syringe, the needle cover contains dry natural latex rubber, but the plunger for the syringe contains no rubber of any kind.

Allergic reactions have been reported rarely in the French post-marketing experience (see **ADVERSE REACTIONS** section).

If Typhim Vi is administered to immunosuppressed persons or persons receiving immunosuppressive therapy, the expected immune response may not be obtained. This includes patients with asymptomatic or symptomatic HIV-infection, severe combined immunodeficiency, hypogammaglobulinemia, or agammaglobulinemia; altered immune states due to diseases such as leukemia, lymphoma, or generalized malignancy; or an immune system compromised by treatment with corticosteroids, alkylating drugs, antimetabolites or radiation.[17]

As with any intramuscular injection, Typhim Vi should be given with caution to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection (see **DRUG INTERACTIONS** section).

PRECAUTIONS

GENERAL

Care is to be taken by the health-care provider for the safe and effective use of Typhim Vi.

EPINEPHRINE INJECTION (1:1000) MUST BE IMMEDIATELY AVAILABLE FOLLOWING IMMUNIZATION SHOULD AN ANAPHYLACTIC OR OTHER ALLERGIC REACTIONS OCCUR DUE TO ANY COMPONENT OF THE VACCINE.

Prior to an injection of any vaccine, all known precautions should be taken to prevent adverse reactions. This includes a review of the patient's history with respect to possible hypersensitivity to the vaccine or similar vaccines, and to possible sensitivity to dry natural latex rubber.

Acute infection or febrile illness may be reason for delaying use of Typhim Vi except when in the opinion of the physician, withholding the vaccine entails a greater risk.

A separate, sterile syringe and needle or a sterile disposable unit must be used for each patient to prevent the transmission of infectious agents from person to person. Needles should not be recapped and should be properly disposed.

Special care should be taken to ensure that Typhim Vi is not injected into a blood vessel.

Safety and immunogenicity data from controlled trials are not available for Typhim Vi following previous immunization with whole-cell typhoid or live, oral typhoid vaccine (See **ADVERSE REACTIONS** section).

INFORMATION FOR PATIENTS

Patients, parents or guardians should be fully informed of the benefits and risks of immunization with Typhim Vi.

Prior to administration of Typhim Vi, patients, parents and guardians should be asked about the recent health status of the patient to be immunized.

Typhim Vi is indicated in persons traveling to endemic or epidemic areas. Current CDC advisories should be consulted with regard to specific locales.

Travelers should take all necessary precautions to avoid contact with or ingestion of contaminated food and water.

One dose of vaccine should be given at least 2 weeks prior to expected exposure.

An optimal reimmunization schedule has not been established. Reimmunization consisting of a single-dose for US travelers every two years under conditions of repeated or continued exposure to the *S. typhi* organism is recommended at this time.

As part of the child's or adult's immunization record, the date, lot number and manufacturer of the vaccine administered should be recorded.[18]

The US Department of Health and Human Services has established a new Vaccine Adverse Event Reporting System (VAERS) to accept reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events required by the National Childhood Vaccine Injury Act of 1986.[19,20] The toll-free number for VAERS forms and information is 1-800-822-7967.[18]

DRUG INTERACTIONS

There are no known interactions of Typhim Vi with drugs or foods.

No studies have been conducted in the US to evaluate interactions or immunological interference between the concurrent use of Typhim Vi and drugs (including antibiotics and antimalarial drugs), immune globulins or common traveler's vaccines (e.g., vaccines for tetanus, poliomyelitis, yellow fever and meningococcus). (See **ADVERSE REACTIONS** section.)

As with other intramuscular injections, Typhim Vi should be given with caution to individuals on anticoagulant therapy.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

Typhim Vi has not been evaluated for its carcinogenic potential, mutagenic potential or impairment of fertility.

PREGNANCY

REPRODUCTIVE STUDIES – PREGNANCY CATEGORY C

Animal reproduction studies have not been conducted with Typhim Vi. It is not known whether Typhim Vi can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Typhim Vi should be given to a pregnant woman only if clearly needed.[21]

When possible, delaying vaccination until the second or third trimester to minimize the possibility of teratogenicity is a reasonable precaution.[14]

NURSING MOTHERS

It is not known if Typhim Vi is excreted in human milk.

There is no data to warrant the use of this product in nursing mothers for passive antibody transfer to an infant.

PEDIATRIC USE

Safety and effectiveness of Typhim Vi have been established in children 2 years of age and older.[10,11] (See **DOSAGE AND ADMINISTRATION** section.) FOR CHILDREN BELOW THE AGE OF 2 YEARS, SAFETY AND EFFECTIVENESS HAVE NOT BEEN ESTABLISHED.

ADVERSE REACTIONS

Safety of Typhim Vi, the US licensed liquid formulation, has been assessed in clinical trials in more than 4,000 subjects both in countries of high and low endemicity. In addition, the safety of the lyophilized formulation has been assessed in more than 6,000 individuals. The adverse reactions were predominately minor and transient local reactions. Local reactions such as injection site pain, erythema and induration almost always resolved within 48 hours of vaccination. Elevated oral temperature, above 38°C (100.4°F), was observed in approximately 1% of vaccinees in all studies. No serious or life-threatening systemic events were reported in these clinical trials.[10,11]

Adverse reactions from two trials evaluating Typhim Vi lots in the US (18- to 40-year-old adults) are summarized in TABLE 3. No severe or unusual side effects were observed. Most subjects reported pain and/or tenderness (pain upon direct pressure). Local adverse experiences were generally limited to the first 48 hours.[10,11]

TABLE 3.[10,11] **PERCENTAGE OF 18- TO 40-YEAR-OLD US ADULTS PRESENTING WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 48 HOURS AFTER THE FIRST IMMUNIZATION WITH TYPHIM Vi**

REACTION	Trial 1 Placebo N = 54	Trial 1 Typhim Vi N = 54 (1 Lot)	Trial 2 Typhim Vi N = 98 (2 Lots combined)
Local			
Tenderness	7 (13.0%)	53 (98.0%)	95 (96.9%)
Pain	4 (7.4%)	22 (40.7%)	26 (26.5%)
Induration	0	8 (14.8%)	5 (5.1%)
Erythema	0	2 (3.7%)	5 (5.1%)
Systemic			
Malaise	8 (14.8%)	13 (24.0%)	4 (4.1%)
Headache	7 (13.0%)	11 (20.4%)	16 (16.3%)
Myalgia	0	4 (7.4%)	3 (3.1%)
Nausea	2 (3.7%)	1 (1.9%)	8 (8.2%)
Diarrhea	2 (3.7%)	0	3 (3.1%)
Feverish (subjective)	0	6 (11.1%)	3 (3.1%)
Fever ≥100°F	0	1 (1.9%)	0
Vomiting	0	1 (1.9%)	0

No studies were conducted in US children. Adverse reactions from a trial in Indonesia in children one to twelve years of age are summarized in TABLE 4.[10,11] No severe or unusual side effects were observed.

TABLE 4.[10,11] **PERCENTAGE OF INDONESIAN CHILDREN ONE TO TWELVE YEARS OF AGE PRESENTING WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 48 HOURS AFTER THE FIRST IMMUNIZATION WITH TYPHIM Vi**

REACTIONS	N=175
Local	
Soreness	23 (13.0%)
Pain	25 (14.3%)
Erythema	12 (6.9%)
Induration	5 (2.9%)
Impaired Limb Use	0
Systemic	
Feverishness*	5 (2.9%)
Headache	0
Decreased Activity	3 (1.7%)

* Subjective feeling of fever.

In the US Reimmunization Study, subjects who had received Typhim Vi 27 or 34 months earlier, and subjects who had never previously received a typhoid vaccination, were randomized to placebo or Typhim Vi, in a double-blind study. Safety data from the US Reimmunization Study are presented in TABLE 5.[10,11,13] In this study 5/30 (17%) primary immunization subjects and 10/45 (22%) reimmunization subjects had an objective local reaction. No severe or unusual side effects were observed. Most subjects reported pain and/or tenderness (pain upon direct pressure). Local adverse experiences were generally limited to the first 48 hours.[10,11,13]

TABLE 5.[10,11,13] **US REIMMUNIZATION STUDY, SUBJECTS PRESENTING WITH LOCAL AND SYSTEMIC REACTIONS WITHIN 48 HOURS AFTER IMMUNIZATION WITH TYPHIM Vi**

REACTIONS	PLACEBO (N=32)	FIRST IMMUNIZATION (N=30)	REIMMUNIZATION (N=45*)
Local			
Tenderness	2 (6%)	28 (93%)	44 (98%)
Pain	1 (3%)	13 (43%)	25 (56%)
Induration	0	5 (17%)	8 (18%)
Erythema	0	1 (3%)	5 (11%)
Systemic			
Malaise	1 (3%)	11 (37%)	11 (24%)
Headache	5 (16%)	8 (27%)	5 (11%)
Myalgia	0	2 (7%)	1 (2%)
Nausea	0	1 (3%)	1 (2%)
Diarrhea	0	0	1 (2%)
Feverish (subjective)	0	3 (10%)	2 (4%)
Fever ≥100°F	1 (3%)	0	1 (2%)
Vomiting	0	0	0

* At 27 or 34 months following a previous dose given in different studies.

Post-marketing data from foreign countries are available. During the first 5.5 years following approval of Typhim Vi in France, approximately 3.89 million doses were distributed in France. An additional 10.8 million doses have been distributed to other countries worldwide. Reports of adverse events were received either by the French post-marketing surveillance system, which utilizes spontaneous reporting of adverse events, or directly by Aventis Pasteur; 56 and 16 reports were received, respectively, from French and other foreign distribution. Local events reported included erythema, induration and/or pain at the injection site and lymphadenopathy. Systemic events reported included fever, flu-like episode, headache, cervical pain, vomiting, diarrhea, abdominal pain, tremor, hypotension, loss of consciousness, allergic type reactions including urticaria, and other events described below.[10,11]

In the French post-marketing experience, there was one report of diffuse arthralgias and fever two weeks post-vaccination in a 44-year-old female who had also received Hepatitis B vaccine simultaneously; one report of glomerulonephritis seven days post-vaccination in a 23-year-old male who had also received BCG vaccine; one report of neutropenia in a 29-year-old female two days post-vaccination who had also received yellow fever vaccine; one report of bilateral retinitis three weeks post-vaccination in a 26-year-old male who had also received Hepatitis B vaccine; and one report of polyarthritis four days post-vaccination in an 18-year-old male who had also received Meningococcal Groups A + C vaccine and DT Polio (Diphtheria Tetanus Poliomyelitis) vaccine combination manufactured by Aventis Pasteur.[10,11]

In the French post-marketing experience, the most severe allergic-type reaction occurred in a 24-year-old female with known multiple allergies who had previously received two complete series with a whole-cell typhoid vaccine; she experienced sweats, myalgia and difficulty breathing starting two hours after an IM injection (deltoid) of Typhim Vi. She received 10 mg hydrocortisone and did not require hospitalization.[10,11]

Reporting of Adverse Events

Reporting by parents and patients of all adverse events occurring after vaccine administration should be encouraged. Adverse events following immunization with vaccine should be reported by the health-care provider to the US Department of Health and Human Services (DHHS) Vaccine Adverse Event Reporting System (VAERS). Reporting forms and information about reporting requirements or completion of the form can be obtained from VAERS through a toll-free number 1-800-822-7967.[18]

Health-care providers also should report these events to the Director of Scientific and Medical Affairs, Aventis Pasteur Inc., Discovery Drive, Swiftwater, PA 18370, or call 1-800-822-2463.

DOSAGE AND ADMINISTRATION

Parenteral drug products should be inspected visually for particulate matter and/or discoloration prior to administration. If either of these conditions exist, the vaccine should not be administered.

For intramuscular use only. Do NOT inject intravenously.

Typhim Vi vaccine is indicated for persons two years of age and older.

The immunizing dose for adults and children is a single injection of 0.5 mL. The dose for adults is given intramuscularly in the deltoid, and the dose for children is given IM either in the deltoid or the vastus lateralis. The vaccine should not be injected into the gluteal area or areas where there may be a nerve trunk.

A reimmunizing dose is 0.5 mL. An optimal reimmunization schedule has not been established. Reimmunization consisting of a single dose for US travelers every two years under conditions of repeated or continued exposure to the *S. typhi* organism is recommended at this time.

The skin at the site of injection first should be cleansed and disinfected. Tear off upper aluminum seal of cap. Cleanse top of rubber stopper of the vial with a suitable antiseptic and wipe away all excess antiseptic before withdrawing vaccine.

For single dose syringes, thread the plunger rod into stopper until the plunger rod bottoms out against the stopper and resistance is felt. Do not over tighten the plunger rod.

A separate, sterile syringe and needle or a sterile disposable unit should be used for each patient to prevent transmission of infectious agents from person to person. Needles should not be recapped and should be properly disposed.

There are no data on the safety and efficacy of Typhim Vi administered with any jet injector apparatus and this method of delivery is not recommended.

HOW SUPPLIED

Syringe, 0.5 mL – Product No. 49281-790-01
Vial, 20 Dose (Available on special contract basis only.) – Product No. 49281-790-20
Vial, 50 Dose (Available on special contract basis only.) – Product No. 49281-790-50

STORAGE

Store between 2°– 8°C (35°– 46°F). DO NOT FREEZE.

REFERENCES

1. Levine MM, et al. New knowledge on pathogenesis of bacterial enteric infections as applied to vaccine development. Microbiol. Rev. 47: 510 - 550, 1983
2. Levine MM. Typhoid Fever Vaccines. p 333-361. In Vaccines, Plotkin SA, Mortimer EA, eds. W.B. Saunders, 1988
3. Levine MM, et al. Typhoid Fever Chapter 5, In: *Vaccines and Immunotherapy*. Stanley J. Cryz, Jr., Editor. pp 59-72, 1991
4. CDC. Summary of Notifiable Diseases, United States 1992. MMWR 41: No. 55, 1993
5. Ryan CA, et al. *Salmonella typhi* infections in the United States, 1975-1984: Increasing Role of Foreign Travel. Rev Infect Dis 11:1-8, 1989
6. Woodruff BA, et al. A new look at typhoid vaccination. Information for the practicing physician. JAMA 265: 756-759, 1991
7. Ames WR, et al. Age and sex as factors in the development of the typhoid carrier state, and a method for estimating carrier prevalence. Am J Public Health 33: 221-230, 1943
8. CDC. Typhoid fever - Skagit County, Washington. MMWR 39: 749-751, 1990
9. Acharya IL, et al. Prevention of typhoid fever in Nepal with the Vi capsular polysaccharide of *Salmonella typhi*. N Engl J Med 317: 1101-1104, 1987
10. Unpublished data available from Aventis Pasteur Inc., compiled 1991
11. Unpublished data available from Aventis Pasteur SA
12. Klugman KP, et al. Protective activity of Vi capsular polysaccharide vaccine against typhoid fever. The Lancet, 1165-1169, 1987
13. Keitel WA, et al. Clinical and serological responses following primary and booster immunization with *Salmonella typhi* Vi capsular polysaccharide vaccines. Vaccine 12: 195-199, 1994
14. Recommendations of the Advisory Committee on Immunization Practices (ACIP): Update on Adult Immunization. MMWR 40: No. RR-12, 1991
15. CDC. Health Information for International Travel 1992. U. S. Department of Health and Human Services, Public Health Service
16. Recommendations of the Immunization Practices Advisory Committee (ACIP). Typhoid Immunization. MMWR 39: No. RR-10, 1990
17. ACIP: Use of vaccines and immune globulins in persons with altered immunocompetence. MMWR 42: No. RR-4, 1993
18. CDC. Vaccine Adverse Event Reporting System – United States. MMWR 39: 730-733, 1990
19. National Childhood Vaccine Injury Act: Requirements for permanent vaccination records and for reporting of selected events after vaccination. MMWR 37: 197-200, 1988
20. National Childhood Vaccine Injury Act of 1986 (Amended 1987)
21. Recommendations of the ACIP. General recommendations on immunization. MMWR 43: No. RR-14, 1994

Product Information as of June 1995

Manufactured by:
Aventis Pasteur SA
Lyon France
US Gov't License #1279

Distributed by:
Aventis Pasteur Inc.
Swiftwater PA 18370 USA
1-800-VACCINE (1-800-822-2463)

Aventis Pasteur

Aventis