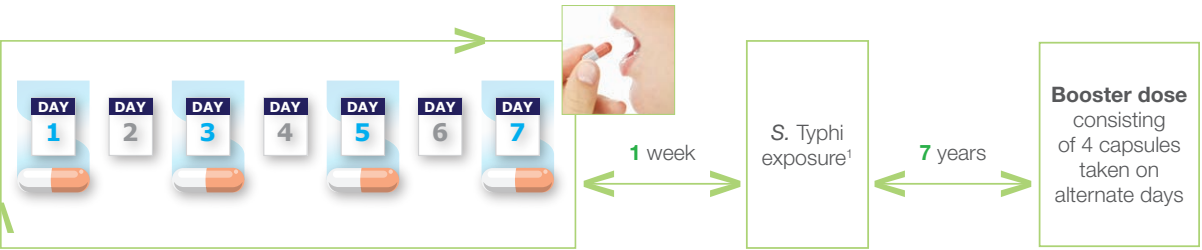


Vivotif® dosage and administration



- 4 capsules taken on alternate days, e.g., one capsule on days 1, 3, 5 and 7¹
- The vaccine is to be taken approximately one hour before, or two hours after a meal¹
- Capsules should be taken with at least 4 oz of cool or lukewarm water (temperature not to exceed body temperature, e.g., 37°C [98.6°F])¹
- Capsules should not be chewed but swallowed as soon as possible after placing in the mouth¹
- Dosing must be completed at least 1 week prior to S. Typhi exposure¹
- Unless a complete immunization schedule is followed, an optimum immune response may not be achieved
- The optimum booster schedule for Vivotif® has not been determined. Protective efficacy has been shown to persist for at least 7 years.¹
- A booster dose should be given if repeated/continued exposure to typhoid fever¹†
 - 4 capsules taken on alternate days every 7 years¹

Not all recipients of Vivotif® will be fully protected against typhoid fever. Travellers should take all necessary precautions to avoid contact with or ingestion of potentially contaminated food or water.¹,⁴

Storage and stability¹

- Vivotif® should be shipped and stored at refrigerated temperatures between 2°C and 8°C (35.6°F and 46.4°F). Vaccine capsules should be stored in the refrigerator between doses. DO NOT FREEZE.
- Each blister of vaccine shows an expiration date. This expiration date is valid only if the product has been maintained between 2°C and 8°C (35.6°F and 46.4°F).
- The product should be stored in a dry place and protected from light.

†Note that there is no experience with the vaccine as a booster for persons previously vaccinated with parenteral typhoid vaccine.¹

Guide your patients on how to take Vivotif®

DO's

Do complete the 4-capsule dosing at least 1 week before travelling¹

Do take each capsule on an empty stomach (1 hour before eating or 2 hours after eating)¹

Do take each capsule with a full glass of cool or lukewarm water¹

Do keep capsules in refrigerator¹

DON'Ts

Don't take Vivotif® while you are taking antibiotics; Vivotif® should not be taken within 3 days before or after treatment with antibiotics (consult your doctor)¹

Don't take Vivotif® with alcohol (alcoholic beverages should not be consumed one hour before or two hours after taking Vivotif®)¹

Don't open or chew capsules¹

Don't forget to skip a day between capsules¹

Don't forget to take all 4 capsules¹



HELP PROTECT YOUR PATIENTS against typhoid fever

Vivotif® (Typhoid vaccine live oral attenuated Ty21a) is indicated for immunization of adults and children against disease caused by *Salmonella* Typhi (new nomenclature: *Salmonella enterica* subspecies *enterica* serovar Typhi).¹

Results from clinical studies indicate that adults and children 5 years and older may be protected against typhoid fever following the oral ingestion of 4 doses of Vivotif® (enteric-coated capsules).¹

Immunization (ingestion of all 4 capsules) should be completed at least 1 week prior to exposure to S. Typhi.¹

Not all recipients of Vivotif® will be fully protected against typhoid fever. Travellers should take all necessary precautions to avoid contact with or ingestion of potentially contaminated food or water.¹

Vivotif® will not afford protection against enteric organisms other than S. Typhi.¹

†Comparative clinical significance is unknown.

Vivotif®

Typhoid Vaccine Live Oral Ty21a¹

The only oral vaccine for protection against typhoid fever¹,²†

Typhoid fever

Typhoid fever is a systemic infection caused by the bacterium *Salmonella* Typhi usually through ingestion of contaminated food or water.²

Typhoid fever is a systemic illness of varying severity. The clinical course ranges from mild illness with low-grade fever to severe systemic disease with abdominal perforation and extra-intestinal infection.²

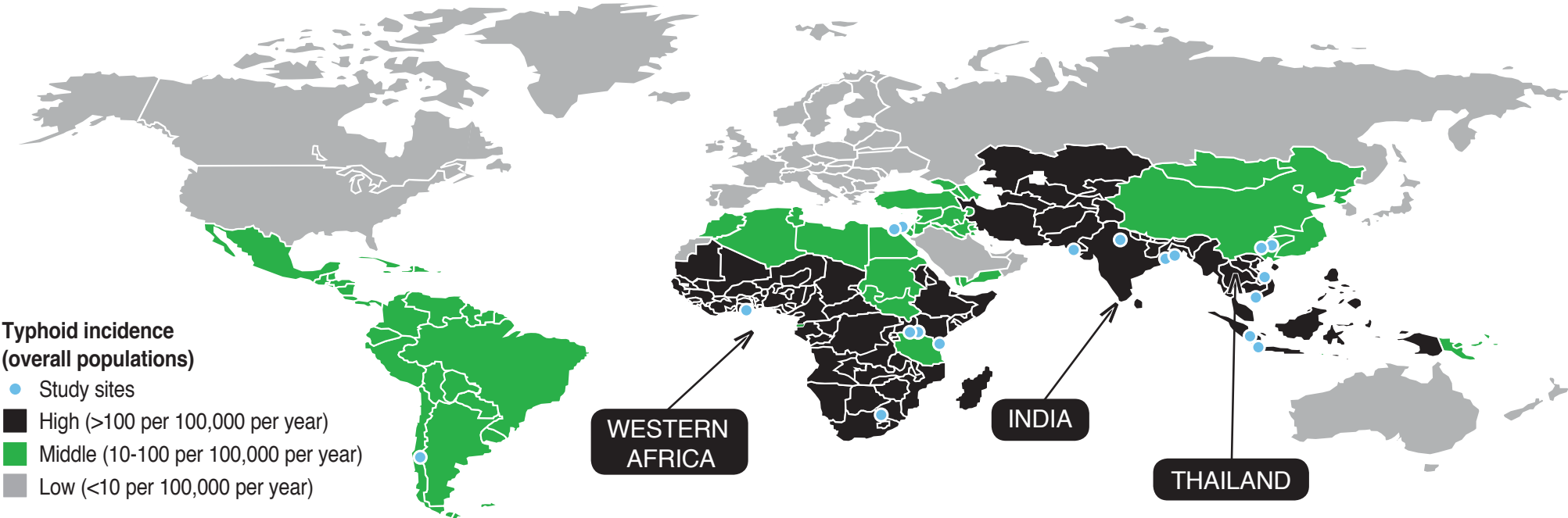
According the World Health Organization (WHO), 21 million cases and 222,000 typhoid-related deaths occur annually worldwide.^{2†}

In Canada, where most cases of typhoid occur in travellers, there was a mean of 144 cases of typhoid reported annually (2004 to 2013), with a mean incidence rate of 0.43 per 100,000 population.²

† Vivotif® is not indicated to treat or reduce the consequences of typhoid fever following onset of the condition.



Typhoid incidence in low- and middle-income countries (2010)^{3‡}



‡ Risk adjusted and corrected for blood culture sensitivity.

Vivotif® demonstrated effective protection against typhoid fever¹

- In a study in North American volunteers, protective efficacy of 87% was demonstrated in vaccinated versus control group after challenge with virulent *S. Typhi* ($p = 0.0002$).
- Because of the very low incidence of typhoid fever in residents of North America, efficacy studies are not currently feasible in this population. However, the above observations support the expectation that Vivotif® will provide protection to recipients from non-endemic areas, such as the United States and Canada.

Vivotif® has an established safety and tolerability profile

- No serious adverse systemic reactions reported in clinical trials¹
- In clinical trials, nausea and rash occurred more frequently in vaccine recipients vs. placebo group¹
- Reported adverse reactions include:¹
 - Nausea, abdominal pain, vomiting, diarrhea, fever, headache, skin rash or urticaria on the trunk and/or extremities (all frequent: >1/100, <1/10)
- Experience from postmarketing surveillance has confirmed that adverse reactions are rare¹



Clinical Use:

Routine typhoid vaccination is not recommended in Canada but immunization should be considered in the following situations:¹

- 1) travel in endemic areas for extended periods, or off the usual tourist tracks;
 - 2) on-going household or intimate exposure to a typhoid carrier;
 - 3) laboratory workers who frequently handle cultures of *S. Typhi*.
- Not all recipients of Vivotif® will be fully protected against typhoid fever. Travellers should take all necessary precautions to avoid contact with or ingestion of potentially contaminated food or water.

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

Vivotif® will not afford protection against enteric organisms other than *S. Typhi*.¹

An optimal booster dose has not yet been established. However, it is recommended that a booster dose consisting of 4 capsules taken on alternate days be given every 7 years under conditions of repeated or continued exposure to typhoid fever.¹

Typhoid fever continues to be an important disease in many parts of the world. Travellers entering such areas are at risk of contracting typhoid fever following the ingestion of contaminated food or water.¹

Geriatrics: No data available.¹

Pediatrics (<5 years of age): The efficacy of Vivotif® (enteric-coated capsules) has not been established in children under 5 years of age. The capsule formulation is therefore not recommended for use in children under 5 years of age.¹

Contraindications:¹

- Hypersensitivity to any component of the vaccine or the enteric-coated capsule. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the Product Monograph.
- Safety of the vaccine has not been demonstrated in persons deficient in their ability to mount a humoral or cell-mediated immune response due to either a congenital or acquired immunodeficient state, including treatment with immunosuppressive or antimitotic drugs. The vaccine should not be administered to these persons regardless of benefits.

Other relevant warnings and Precautions:¹

- **General:** The vaccine should not be administered to persons during an acute febrile illness.
- **Gastrointestinal:** The vaccine should not be administered to persons during an acute gastrointestinal illness.
- **Pregnant Women:** It is not known whether Vivotif® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Vivotif® should be given to a pregnant woman only if clearly needed.

- **Nursing Women:** There are no data to support the use of this product in nursing mothers. It is not known if Vivotif® is excreted in human milk.
- **Pediatrics (<5 years of age):** The capsule formulation is not recommended for use in children under 5 years of age.

Drug Interactions:¹

Antibiotics: Because the growth of vaccine organisms may be inhibited by the concomitant intake of sulfonamides or antibiotics, vaccination should be started at least three days after treatment with these agents. Accordingly, therapy with sulfonamides or antibiotics should preferably be started at least three days after the last dose of Vivotif®.

Alcohol: Alcoholic beverages should not be consumed one hour before or two hours after taking Vivotif®.

Antimalarials: When planning malaria prophylaxis as well as typhoid prophylaxis, the fixed combinations of atovaquone and proguanil hydrochloride or pyrimethamine and sulfadoxine can be given concomitantly with Vivotif®. Likewise, the administration of Vivotif® and mefloquine or chloroquine can be given concomitantly.

When using any other antimalarial, immunization with Vivotif® should precede antimalarial prophylaxis. The interval between the last Vivotif® dose and the beginning of malaria prophylaxis should generally be three days.

Other vaccines: The concomitant administration of oral polio vaccine or yellow fever vaccine did not suppress the immune response elicited by *S. Typhi* Ty21a vaccine strain.

There is no reason to believe that simultaneous administration of parenteral vaccines or immunoglobulins with Vivotif® will decrease vaccine efficacy.

For more information:

Please consult the Vivotif® Product Monograph at pdf.hres.ca/dpd_pm/00047876.PDF for important information relating to adverse reactions and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling Emergent BioSolutions medical information services at 1-844-202-1232.

References:

1. Vivotif® Product Monograph, October 23, 2018.
2. Canadian Immunization Guide – Typhoid Vaccine. Available at: <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-typh-eng.php#approve>. Accessed November 11, 2019.
3. Mogasale V *et al.* Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. *The Lancet Global Health* 2014; 2(10):e570-e580.
4. Centers for Disease Control and Prevention website. Chapter 3. Infectious Diseases Related to travel. Typhoid & Paratyphoid Fever. <https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/typhoid-paratyphoid-fever>. Accessed November 11, 2019.



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