

# VIVOTIF<sup>®</sup> Oral

## Product Information

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### NAME OF THE MEDICINE

Oral Typhoid Vaccine

### DESCRIPTION

Vivotif<sup>®</sup> Oral is an oral, live, attenuated typhoid vaccine for active immunisation against typhoid and contains *Salmonella typhi* strain Ty21a. Each enteric coated capsule contains not fewer than  $2 \times 10^9$  viable organisms. Each capsule also contains the following excipients: ethylene glycol, sucrose, ascorbic acid, protein hydrolysate, lactose, magnesium stearate, hypromellose phthalate, gelatin (bovine derived), titanium dioxide, erythrosine ci45430, iron oxide yellow ci77492, iron oxide red ci77491, dibutyl phthalate, diethyl phthalate. The manufacture of this product includes exposure to bovine derived material. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

Vivotif<sup>®</sup> Oral capsules are salmon pink and white in colour.

### PHARMACOLOGY

The attenuated Ty21a strain is a mutant of *Salmonella typhi*, which is deficient in the enzyme UDP-4-galactose epimerase. This results in the organisms being unable to effectively metabolize galactose. When grown in the presence of adequate amounts of galactose, the organism accumulates galactose-containing metabolites and ultimately undergoes spontaneous lysis. In the presence of a restricted supply of galactose the organism develops the smooth lipopolysaccharide coat believed to be necessary for immune response. In the intestine, where galactose is normally present, it is however unable to survive for long. The vaccine strain cannot be detected in the stools after 3 days following oral ingestion.

### CLINICAL TRIALS

In one clinical study conducted in Egypt, in children above 6 years of age, oral ingestion of the vaccine as a solution preceded by a dose of sodium bicarbonate to reduce gastric activity (in order to reduce lysis of the organism in the stomach), provided approximately 95% protection against typhoid. In another study, conducted in Chile, enteric coated capsules provided approximately 70% protection. The duration of protection conferred by Vivotif<sup>®</sup> Oral remains to be fully established. However, repeat vaccination is not considered necessary within 12 months after initial vaccination See **DOSAGE AND ADMINISTRATION**.

### INDICATIONS

Vivotif<sup>®</sup> Oral is indicated for active immunisation against typhoid in adults and children above 6 years of age. Effectiveness in children below 6 years of age is not known at present.

### CONTRAINDICATIONS

Primary and acquired immunodeficiency, including that from treatment with immunosuppressive and antimetabolic drugs, acute febrile illness: acute intestinal

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infection, allergic reactions to a previous dose, and hypersensitivity to the vaccine or to any of the inactive components.

### **PRECAUTIONS**

No data are currently available about the efficacy of Vivotif<sup>®</sup> Oral in individuals with blood dyscrasias, leukaemia, lymphoma or any type of malignant neoplasm affecting the bone marrow or lymphatic system. These individuals may fail to develop protection because of their disturbed immune functions.

In the case of acute febrile illnesses and acute gastro-intestinal illness as well as during and up to 3 days after treatment with antibiotics, Vivotif<sup>®</sup> Oral should not be taken due to possible inhibition of the growth of the vaccine organisms.

The capsules must be swallowed whole and not chewed because of the destruction of the organism by gastric acid.

See also **INTERACTIONS WITH OTHER MEDICINES**.

### **Use in Pregnancy - Category B2**

Studies in animals are inadequate but available data show no evidence of an increased occurrence of foetal damage.

### **INTERACTIONS WITH OTHER MEDICINES**

The vaccine should not be administered concurrently with antibiotics or other drugs (e.g. sulphonamides) that are active against salmonellae. The vaccine should be administered first and at least 3 days should elapse between the final dose of the vaccine and such drugs.

The simultaneous administration of Vivotif<sup>®</sup> Oral Typhoid Vaccine and parenteral (live attenuated) yellow fever vaccine, or inactivated vaccines, or oral polio vaccines, or parenteral immunoglobulin preparations, has been reported not to interfere with the immune response.

### **Anti-Malaria Prophylaxis**

#### General

In the case of planned anti-malarial prophylaxis, immunisation with Vivotif<sup>®</sup> Oral Typhoid Vaccine should precede anti-malaria prophylaxis. The interval between the last dose of Vivotif<sup>®</sup> Oral Typhoid Vaccine and the beginning of anti-malarial prophylaxis should, in general, be at least 3 days.

If anti-malaria prophylaxis has been started, the minimum interval between the last dose of anti-malaria prophylaxis and the first dose of Vivotif<sup>®</sup> Oral Typhoid Vaccine should be at least 3 days.

This 3-day interval should generally be regarded as optimal.

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### Chloroquine and/or pyrimethamine/sulfadoxine

Vivotif® Oral Typhoid Vaccine can be given with chloroquine and/or pyrimethamine/sulfadoxine. In these studies, the anti-malarials were given first, followed 12 hours later by Vivotif® Oral Typhoid capsule.

### Mefloquine

Mefloquine can be given concomitantly with Vivotif® Oral Typhoid Vaccine. A lower IgG response was observed compared to taking Vivotif® Oral Typhoid Vaccine alone, however the immune response was not affected and vaccine efficacy was not compromised.

### Atavaquone and Proguanil, fixed combination

Atavaquone and proguanil (fixed combination formulation) may be given concomitantly with Vivotif® Oral Typhoid Vaccine.

### Proguanil

Proguanil, when given alone, should be administered only if 10 days or more have elapsed since the final dose of Vivotif® Oral Typhoid Vaccine.

## **ADVERSE EFFECTS**

### **Clinical Trials**

The following adverse effects were reported as common (in accordance with CIOMS definition of <1/10 and >1/100) and were generally mild – constipation, abdominal cramps, diarrhoea, nausea, vomiting, anorexia, fever, headache and urticarial exanthema.

### **Post-marketing Data**

The following additional adverse effects have been reported very rarely (CIOMS definition: <1/10,000) during post-marketing surveillance.

Skin reactions such as dermatitis, exanthema, pruritus and urticaria, anaphylaxis, asthenia, malaise, tiredness, shivering, paraesthesia, dizziness, arthralgia and myalgia.

## **DOSAGE AND ADMINISTRATION**

The complete immunisation schedule, irrespective of age, for adults and children above 6 years of age, is the ingestion of one capsule on each of days 1, 3 and 5.

The Vivotif Oral Typhoid Vaccine capsule should be swallowed whole and must not be chewed. The capsule should be taken approximately one hour before a meal, with a cold or lukewarm (temperature not to exceed body temperature i.e. 37°C [98.6°F]) drink.

### **Re-immunisation**

An optimal booster schedule for Vivotif® Oral Typhoid Vaccine has not been determined. Re-immunisation, consisting of 3 capsules, one taken on each of Days 1, 3 and 5 is recommended every 3 years.

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See also “**INTERACTIONS WITH OTHER MEDICINES.**”

### **OVERDOSAGE**

Doses five-fold higher than the recommended dose caused only mild, mainly gastro-intestinal adverse reactions which did not require medical treatment. Overdosing can increase the possibility of shedding *S. typhi* Ty21a organism in the faeces.

For information on the management of overdose, contact the Poison information Centre on 13 11 26 in Australia or 0800 POISON (0800 764 766) in New Zealand.

### **PRESENTATION AND STORAGE CONDITIONS**

Store between +2 and +8°C in a dry place and protected from light. Every package shows an expiry date and the product should not be used after this date.

Each carton contains 3 capsules in a blister pack. Each enteric coated capsule contains not fewer than  $2 \times 10^9$  viable organisms of *Salmonella typhi* strain Ty21a.

### **NAME AND ADDRESS OF THE SPONSOR**

#### **Australia**

Seqirus Pty Ltd  
ABN 26 160 735 035  
63 Poplar Road  
Parkville, VIC 3052  
Australia

#### **New Zealand**

Seqirus (NZ) Ltd  
PO Box 62 590  
Greenlane  
Auckland 1546  
New Zealand

### **POISONS SCHEDULE OF THE MEDICINE**

Prescription Only Medicine (S4)

### **Date of first inclusion in the Australian Register of Therapeutic Goods**

3 April 2009

### **Date of most recent amendment**

2 February 2017

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