AUSTRALIAN PRODUCT INFORMATION – VIVOTIF ORAL (SALMONELLA TYPHI) CAPSULE

1 NAME OF THE MEDICINE

Oral Typhoid Vaccine *Salmonella typhi* strain Ty21a (live, attenuated)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Vivotif® 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 x 10^9 viable organisms.

Excipients with known effect: Vivotif® Oral contains sucrose and lactose. It may also contain traces of sulfites and milk products.
For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Vivotif® Oral capsules are enteric-coated capsules, salmon-pink and white in colour.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Vivotif® 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.

4.2 DOSE AND METHOD OF 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 drink (temperature not to exceed body temperature i.e. 37ºC) .

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.

See also Section 4.5 Interaction with other medicines and other forms of interaction.

4.3 CONTRAINDICATIONS

Primary and acquired immunodeficiency, including that from treatment with immunosuppressive and antimitotic drugs, acute febrile illness: acute intestinal infection, allergic reaction to a previous dose, and hypersensitivity to the vaccine or to any of the inactive components.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

No data are currently available about the efficacy of Vivotif® 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 compromised 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® 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.

Use in elderly
No data available.

Paediatric use
No data available.

Effects on laboratory tests
No data available.

See also Section 4.5 Interaction with other medicines and other forms of interaction.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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® 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® Oral Typhoid Vaccine should precede anti-malaria prophylaxis. The interval between the last dose of Vivotif® 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® Oral Typhoid Vaccine should be at least 3 days.

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

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.

Atavoquone 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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

It is not known whether Vivotif can affect reproductive capacity.

Use in Pregnancy – Category B2

Studies in animals are inadequate but available data show no evidence of an increased occurrence of foetal damage. Vivotif should not be administered during breast-feeding unless clearly needed, like in cases of increased risk of infection.

Use in lactation

There are no data regarding administration of Vivotif to nursing mothers. *S*. Typhi Ty21a is not absorbed systemically, therefore is it not expected to be excreted in human milk. Vivotif should not be administered during breast-feeding unless clearly needed, like in cases of increased risk of infection.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive or use machines have been performed. However, some of the undesirable effects mentioned under section 4.8 may temporarily affect the ability to drive or operate machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE 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.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

Post-marketing Experience

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.

4.9 OVERDOSE

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 Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Bacterial vaccines (J07AP01)

Mechanism of action

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® Oral remains to be fully established. However, repeat vaccination is not considered necessary within 12 months after initial vaccination See **DOSAGE AND ADMINISTRATION.**

5.2 PHARMACOKINETIC PROPERTIES

Not applicable.

5.3 PRECLINICAL SAFETY DATA

No preclinical safety data are available.

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

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, and 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.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

18 months shelf life. Every package shows an expiry date and the product should not be used after this date.

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG).

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store between +2 and +8°C in a dry place and protected from light.

6.5 NATURE AND CONTENTS OF CONTAINER

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

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Not applicable.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

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

9 DATE OF FIRST APPROVAL

3 April 2009

10 DATE OF REVISION

28 November 2019

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SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Reformat as per TGA requirement
4.4, 4.7, 5.1, 5.2, 5.3, 6.1, 6.3, 6.7	Minor editorial changes to improve readability.
4.2, 4.9, 8	Minor editorial changes - updated to make document Australian specific.