NEW ZEALAND DATA SHEET

1 VIVOTIF® Oral

Oral Typhoid Vaccine

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.

For a full list of excipients, see section 6.1.

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 capsule should be swallowed whole and must not be chewed. It should be taken approximately 1 hour before a meal, with a cold or lukewarm drink (temperature not to exceed body temperature i.e. 37°C.

Re-immunisation

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

See also 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 gastrointestinal 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.

4.5 Interaction with other medicines and other forms of interaction

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

Use in Pregnancy: Category B2. Studies in animals are inadequate but available data show no evidence of an increased occurrence of fetal damage.

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 Undesirable effects

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 Experience

The following additional adverse effects have been reported very rarely (CIOMS definition: <1/10,000) during postmarketing 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 gastrointestinal 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 National Poisons Centre on 0800 POISON or 0800 764 766.

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Bacterial vaccines (J07AP01)

5.1 Pharmacodynamic properties

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 metabolise 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.

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 section 4.2 'Dosage and method of Administration'.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No preclinical safety data are 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

Not applicable.

6.3 Shelf life

18 months.

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 three 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

None.

7 MEDICINE SCHEDULE

Prescription-only Medicine.

8 SPONSOR

Biocelect New Zealand Ltd
Level 5, Wynn Williams House
47 Hereford Street
Christchurch 8013
NEW ZEALAND
Telephone:0800 884 980
info@biocelect.com

9 DATE OF FIRST APPROVAL

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10 DATE OF REVISION OF THE TEXT

24 January 2024

VIVOTIF® is a Registered Trademark of Bavarian Nordic A/S, DK.

SUMMARY TABLE OF CHANGES

Section affected	Summary of new information
Section 10	updated trademark attribution to Bavarian Nordic A/S, DK.