SUMMARY OF PRODUCT CHARACTERISTICS
Product Summary

1. Trade Name of the Medicinal Product

Vivotif®

2. Qualitative and Quantitative Composition
The composition in terms of active ingredients is as follows:
- *Salmonella enterica* serovar Typhi (abbr. *S. typhi*) Ty21a not less than 2 x 10^9 viable cells Quantities expressed per capsule.

3. Pharmaceutical Form
Enteric-coated capsule, for oral administration to humans.

Clinical Particulars

4.1 Therapeutic Indications
For active oral immunisation against typhoid fever in children aged 6 years and over, adults and elderly.

4.2 Posology and Method of Administration

Posology

Children aged 6 years and above, *adults and elderly:* One capsule is to be taken on day 1. The second capsule should be taken on day 3 and the third capsule on day 5.

Unless the immunisation schedule of 3 vaccine capsules is completed, an optimal immune response may not be achieved.
Even after three doses, not all recipients of Vivotif will be fully protected against typhoid fever. Therefore, travellers should take all necessary precautions to avoid contact with or ingestion of potentially contaminated food or water.
Protection against typhoid fever commences approximately 7-10 days after ingesting the third dose of vaccine.

Under conditions of repeated or continuous exposure to *S. typhi* protection persists for at least 3 years.
In the case of travel from a non-endemic area to an area where typhoid fever is endemic, an annual booster consisting of three doses is recommended.

Children under 6 years: Safety and efficacy have not been established in children under 6 years of age.

Method of administration

The blister containing the vaccine capsules should be inspected to ensure that the foil seal and capsules are intact.

The capsule should be taken approximately one hour before a meal with a cold or lukewarm (temperature not to exceed body temperature, e.g. 37°C [98.6°F]) drink on alternate days, e.g. days 1, 3 and 5. The vaccine capsule should not be chewed and should be swallowed as soon as possible after placing in the mouth.

4.3 Contra-indications
Vivotif must not be administered:
- To persons known to be hypersensitive to any component of the vaccine or the enteric-coated capsule (see section 6.1).
- To persons with congenital or acquired immune deficiency (including patients receiving immunosuppressive or antimitotic drugs).
- During an acute febrile illness or during an acute gastrointestinal illness. Vaccination should be postponed until after recovery.

4.4 Special Warnings and Precautions for Use
None known.

4.5 Interactions with other Medicaments and other forms of Interaction
As the growth of vaccine organisms may be inhibited by sulphonamides or antibiotics, vaccination should not commence within 3 days after completing treatment with any antibacterial agents. Also, it is preferable that antibacterial therapy should not commence within 3 days after the last dose of Vivotif.

If malaria prophylaxis is also required, the fixed combination of atovaquone and proguanil can be given concomitantly with Vivotif. Doses of mefloquine and Vivotif should be separated by at least 12 hours. For other antimalarials, there should be an interval of at least 3 days between the last dose of Vivotif and the first dose of malaria prophylaxis.

Vivotif may be administered concomitantly with the live attenuated vaccines yellow fever vaccine and oral polio vaccine.

4.6 Pregnancy and Lactation
Animal reproduction studies have not been conducted with Vivotif. It is not known whether Vivotif can cause foetal harm when administered to pregnant women or can affect reproduction capacity. Vivotif should be given to a pregnant woman only if clearly needed.

There are no data regarding administration of Vivotif to nursing mothers. It is not known if Vivotif is excreted in human milk.

4.7 Effects on Ability to Drive and Use Machines
None known.

4.8 Undesirable Effects
The following adverse reactions were reported commonly (<1/10 but >1/100) in clinical studies:

Gastrointestinal disorders
Abdominal pain, nausea, diarrhoea, vomiting

General disorders and administration site conditions
Fever, influenza-like illness

Nervous system disorders
Headache

Skin and subcutaneous tissue disorders
Rash

The following additional adverse reactions have been reported very rarely (approximately <1/10,000) during post-marketing surveillance:
Skin reactions such as dermatitis, exanthema, pruritus, urticaria.
Anaphylaxis.
Asthenia, malaise, tiredness, shivering.
Paraesthesiae, dizziness.
Arthralgia, myalgia.

4.9 Overdose
Doses five-fold higher than the recommended dose do not produce vomiting, abdominal distress or fever. However overdosing can increase the possibility of shedding the *S. typhi* Ty21a organisms in the faeces.

Pharmacological Properties

5.1 Pharmacodynamic Properties
As a result of irreversible changes in cell wall biosynthesis, the Ty21a strain is devoid of pathogenicity but is able to elicit an immune response against *S. typhi*.

Excretion of the vaccine strain after administering doses approximately 50 times greater than those in the present vaccine was assessed by taking stool or rectal swabs daily for 7 days following the last dose of vaccine. The rate of excretion of the vaccine strain in the stools was low, and the vaccine strain could not be recovered from small bowel aspirates one or more days after vaccination. Sera for determination of antibodies to O, H and Vi antigens were obtained prior to vaccination and biweekly for 8 weeks. Fourfold or greater responses in titre of O antibody only were observed.

There was no correlation between faecal excretion of the strain Ty21a organisms and seroconversion with respect to titre of any of the antibodies tested.

5.2 Pharmacokinetic Properties
Not applicable.

5.3 Preclinical Safety Data
There is no other relevant information other than presented in the sections above.

Pharmaceutical Particulars

6.1 List of excipients
The excipients contained in the preparation are as follows:

Sucrose (Saccharose)	Ph. Eur
Ascorbic acid (E300)	Ph. Eur
Casein hydrolysate (Hy-Case SF Sheffield)	HSE
Lactose anhydrous	NF/USP, Ph. Eur.
Magnesium stearate (E470)	Ph. Eur.
Inactivated S. typhi Ty21a bacteria	HSE

Capsule:

Gelatin
Titanium dioxide (white) (E171)
Titanium dioxide (red) (E171)
Erythrosine red No.3 (E127)
Ferric oxide (yellow)
(E172) Ferric oxide (red) (E172)

Capsule coating:

Hydroxypropylmethyl-cellulose- phthalate (HP-MCP) - 50
Ethylene glycol Dibutyl phthalate
Diethyl phthalate

6.2 Incompatibilities
None known.

6.3 Shelf life
In blister packs: 18 months from date of packing, unopened, at 2-8°C. After opening blister: not applicable.

6.4 Special Precautions for Storage
Store at 2-8°C. Protect from light.

6.5 Nature and Contents of Container
Blister packs (PVC/PE/PVDC 250/30/90). Each blister pack contains 3 capsules.

6.6 Instruction for Use/Handling
No special instructions.

Administrative Data

7. Manufacturer
PaxVax Berna GmbH.
Oberriedstrasse 68
3174 Thörishaus
Switzerland

8. Further information
For more information please contact:
Pharmaforte (S) Pte Ltd
6 Tagore Drive #03-11
Singapore 787623

9. Marketing Authorisation Number
SIN 2260P

10. Date of First Authorisation / Renewal of Authorisation
July 5, 1988

11. Date of (Partial) Revision of the Text
April 01, 2016 POM

Legal category
POM