PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Vivotif

Gastro resistant hard capsule

The active ingredient and its quantity:
Each capsule of Vivotif contains not less than $2x10^9$ CFU of:
Viable *Salmonella* Typhi Ty21a cells
For information on inactive ingredients and allergens in the product see section 2- "Important information about some of the ingredients of the medicine" and section 6 –"Further information".
Read all this leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Vivotif is an active oral vaccine against typhoid fever, caused by *Salmonella* Typhi bacteria (*Salmonella* enterica serovar Typhi, (S. Typhi)), in adults and children aged five years and older.
This vaccine should be used in accordance with official recommendations.
Therapeutic group: Bacterial vaccines
How Vivotif works
The vaccine bacteria in Vivotif have been altered so that they cannot cause typhoid fever but still stimulate the body's natural defense system (immune system) to fight typhoid-causing bacteria.
Other types of *Salmonella* illness
There are many other types of *Salmonella* bacteria. Most of these cause illnesses with diarrhoea that are quite different to typhoid fever. They are also less serious. Vivotif cannot protect you against infections due to these other types of Salmonella bacteria.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are hypersensitive (allergic) to the active ingredient or to any of the other ingredients of the medicine (see section 6 in this leaflet).
- You experienced an allergic reaction when taking Vivotif in the past.
- You have a poor immune system for any reason, for example, if you have had poor immunity to infections since birth. You may also have poor immunity due to certain infections or treatments that suppress the immune system - such as: high dose corticosteroids, cancer drugs or radiotherapy.
- You have a high fever (above 38.5°C) or an illness affecting your gut (such as diarrhoea) at the moment- do not take Vivotif until you have recovered.

Special warnings regarding use of the medicine
Not everyone taking a full course of Vivotif will be fully protected against typhoid fever. It is important to continue to adhere to hygiene advice and exercise caution regarding food and water consumed in typhoid-affected areas.
Children
The medicine is not indicated for children under the age of 5 as the efficacy and safety of the medicine at these ages have not been proven.
Drug interactions
If you are taking, or have recently taken, other medicines or other vaccines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist. This is because Vivotif can affect the way some other medicines or vaccines work. In particular if you are taking:
- Antibiotics - Vivotif may not work if it is taken while you are also taking antibiotics. Take Vivotif no earlier than 3 days after the last dose of an antibiotic.
  A longer interval should be considered for long-acting antibiotics (e.g., azithromycin).
- Medicines to prevent malaria - do not start these until 3 days after the last dose of Vivotif unless otherwise directed by your doctor.

Use of medicine and food
Vivotif is taken on an empty stomach and at least one hour before the next meal.
Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
If you are pregnant or breast-feeding do not take Vivotif, unless clearly needed, like in cases of increased risk of infection.
It is not known whether Vivotif causes foetal harm when administered to pregnant women or can affect fertility.
There are no data regarding administration of Vivotif to nursing mothers. S. Typhi Ty21a is not absorbed systemically, therefore it is not expected to be excreted in human milk.
Driving and using machines
It is not known if Vivotif affects your ability to drive or use machines. However, do not drive or use any machines if you are feeling unwell since some of the side effects mentioned under section 4 may temporarily affect the ability to drive or operate machinery.
Important information about some of the ingredients of the medicine
Vivotif contains lactose and sucrose. If you have been told by your doctor that you have an intolerance to some sugars, consult with your doctor before taking Vivotif.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use Vivotif according to the doctor's instructions.
Check with your doctor or pharmacist if you are not sure about the dosage and vaccination regimen of Vivotif.
The dosage and vaccination regimen will be determined by the doctor only. The recommended dose is usually three capsules, and you need to take one capsule every other day, as follows:
- Take the first capsule on a chosen day. This is Day 1.
- Take the second capsule on Day 3.
- Take the third capsule on Day 5.

Do not exceed the recommended dose.
The blister pack containing the vaccine capsules should be inspected to ensure that the foil seal and capsules are intact.
Method of administration:
- Take the capsules on an empty stomach and at least one hour before the next meal.
- Do not crush or chew the capsules, since Vivotif consists of an enteric-coated capsule to protect the bacteria during passage through the stomach.
- Swallow the capsules with cold or lukewarm water (temperature not more than 37°C).
- Swallow the capsules as quickly as possible after placing in your mouth.

Protection against typhoid fever starts at about seven to ten days after taking the course of three capsules. Your doctor or pharmacist will advise you how soon before travelling to have your course of Vivotif.
The entire vaccination regimen should be completed at least one week prior to travel to an endemic area.
Re-vaccination
After three years, you may need to take Vivotif again if you continue to visit areas where typhoid fever occurs. In this case, consult with your doctor or pharmacist.
Re-vaccination comprises the ingestion of three capsules on Days 1, 3, and 5, as for the original vaccination regimen.
If you have accidentally taken a higher dosage
If you took all three doses at once by accident, consult with your doctor or pharmacist. It is unlikely to make you ill but you may not be well protected against typhoid fever.
If a child accidentally swallowed the medicine, immediately proceed to a doctor or to a hospital emergency room and bring the package of this medicine with you.
If you forgot to take Vivotif
If you forgot a dose, take it as soon as you remember. Do not take a double dose. Take the next dose about 48 hours later and consult a doctor.
Adhere to the vaccination regimen recommended by the doctor.
If you stop taking the medicine before the end of vaccination regimen you may not be properly protected against typhoid fever.
Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take the medicine. Wear glasses if you need them.
If you have further questions regarding the use of the medicine, consult a doctor or pharmacist.

4. SIDE-EFFECTS

As with any medicine, the use of Vivotif may cause side effects in some users. Do not be alarmed when reading the list of side effects, you may not experience any of them.
Contact your doctor immediately if you experience the following serious side effects: serious allergic reactions causing swelling of the face or throat and breathlessness and/or a drop in blood pressure and fainting.
Other side effects:
Common side effects (affects up to 1-10 users out of 100)
- stomach pains
- nausea
- vomiting
- diarrhoea
- fever
- headache
- skin redness

Side effects which their frequency is not known (side effects whose frequency has not yet been determined)
- skin irritation, rashes, red or lumpy raised rashes, itching
- weakness
- generally feeling unwell
- shivering
- feeling tired
- pins and needles
- feeling dizzy
- pain in your joints or muscles.
- back pain
- decreased appetite, abdominal gas, bloating
- flu-like illness

If one of the side-effects appear or worsen, or if you suffer from side-effects that were not mentioned in the leaflet, consult your doctor.
Reporting of side effects
Side effects can be reported to the Ministry of Health through link "reporting side effects due to drug treatment" located in the home page of the Ministry of Health website (<u>www.health.gov.il</u>) which refers to online form, or by entering the following link: *https://sideeffects.health.gov.il*
Additionally, you may report to Kamada LTD by email:
<u>pharmacovigilance@kamada.com</u>

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
Do not use after the expiry date (exp. date) that appears on the carton. The expiry date refers to the last day of that month.
<u>Storage conditions:</u>
- Store in a refrigerator (2°C – 8°C).
- Keep the blister pack in the outer carton in order to protect from light.
- Do not use Vivotif if you notice that the blister pack or the capsules are not intact.
- Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

<u>In addition to the active ingredient, this medicine also contains:</u>
Lactose anhydrous, sucrose, magnesium stearate (E470), casein acid hydrolysate, ascorbic acid (E300), inactivated S. typhi Ty21a cells.
Capsule coating: hydroxypropylmethylcellulose phthalate, diethyl phthalate, ethylene glycol.
Capsule cap: gelatin, titanium dioxide (E171), yellow iron oxide (E172), red iron oxide (E172), erythrosine (E127).
Capsule body: gelatin, titanium dioxide (E171).
<u>What does the medicine look like and the contents of the pack:</u>
The pack contains a blister pack with three enteric-coated capsules of Vivotif. The capsules are bicoloured white and orange.
<u>License holder:</u> Kamada Ltd., Beit Kama, Israel.
<u>Manufacturer:</u> Bavarian Nordic Berna GmbH
Oberriedstrasse 68, 3174 Thörishaus, Switzerland

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