VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Typhoid fever is an acute, life-threatening, febrile illness resulting from infection by the bacterium *Salmonella* Typhi. It exhibits a wide range of clinical severity. Classic full blown cases begin with malaise, anorexia, myalgia, and fever that increases in stepwise fashion to reach 102–104°F, abdominal discomfort, and headaches. Severe disease manifestations (e.g. septic shock, coma and hemorrhagic necrosis of the small intestine) are frequent occurrences in countries endemic for typhoid fever.

Travelers to regions endemic for typhoid fever constitute a major group at risk for the disease.

VI.2.2 Summary of treatment benefits

The efficacy of the Ty21a vaccine against typhoid fever was initially explored in adult volunteer challenge studies in the USA (Gilman 1977), which showed 87% (p=0.0002) efficacy against a virulent *S*. Typhi challenge in 55 volunteers. A randomized, double-blind placebo-controlled field efficacy study of a liquid formulation of Ty21a was then conducted in Egypt in 32, 388 schoolchildren (Wahdan 1980, Wahdan 1982) which showed a 96% protection rate against typhoid fever over a 3-year observation period (95% confidence interval (CI) = 77%–99%).

In a randomized, placebo-controlled trial in 82, 543 schoolchildren in Chile, Santiago, Area Norte, one or two doses of vaccine in enteric-coated capsules was found to provide 59% protection over 2 years (Black 1990). In another randomized placebo-controlled trial in 109,594 schoolchildren in Chile, Santiago, Area Occidente, three doses of the enteric-coated formulation administered with an interval of 2 days between doses provided 71% protection over 1 year (95% CI: 35%-87%) 67% protection over 3 years (95% CI = 47%–79%) and 62% protection over 7 years of follow-up (95% CI: 48% - 73%) (Levine 1987, Levine 1999).

VI.2.3 Unknowns relating to treatment benefits

The protective efficacy of Ty21a has been extensively proven in 6 large-scale field trials comprising more than half a million adults and children on different continents (Africa, S. America, Asia) (Wahdan 1980, Wahdan 1982, Black 1990, Levine 1987, Levine 1999, Ferreccio 1989, Levine 1990, Simanjuntak 1991), under conditions of field use in a refugee camp (Reisinger 1994) and in an early controlled challenge study in US healthy adult volunteers (Gilman 1977). Age of participants ranged from 3 to 44. There is no evidence of lack of efficacy in other races or age groups.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Allergic and anaphylactic reactions	In <0.01% of individuals receiving the vaccine, an allergic response was observed such as swelling of the eyelids, or difficulty breathing. Most of these	If an allergic reaction is experienced, a doctor should be contacted immediately for advice and further doses should not be taken.

Risk	What is known	Preventability
	events are self-limiting and resolve without treatment, but severe reactions require emergency medical treatment.	

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
None	

Missing information

Risk	What is known
None	

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Vivotif can be found in the <authority website>

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

List of studies in post authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
None	-	-	-	-

Studies which are a condition of the marketing authorisation

Not applicable.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable, this is the initial RMP for Vivotif.