TYPHERIX® PRODUCT INFORMATION

(*Salmonella typhi* Vi polysaccharide)

DESCRIPTION

TYPHERIX is a colourless, sterile liquid containing the cell surface Vi polysaccharide extracted from *Salmonella typhi* Ty2 strain.

The production of Vi polysaccharide active ingredient involves fermentation of *S. typhi* bacteria followed by extraction/purification of the Vi polysaccharide. Traditional culture methods are used for fermentation of *S. typhi.*

Each 0.5 ml dose of vaccine contains 25 µg of the Vi polysaccharide of *Salmonella typhi* in a sterile isotonic sodium chloride solution. TYPHERIX contains phenol (as preservative), and a phosphate buffer.

The manufacture of this product includes exposure to bovine derived materials. 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.

TYPHERIX meets the World Health Organisation (WHO) requirements for biological substances and conforms with the European Pharmacopoeia monograph on Vi polysaccharide typhoid vaccines. No substance of human origin is used in its manufacture.

CLINICAL PHARMACOLOGY

TYPHERIX induces the production of specific anti-Vi antibodies against *Salmonella typhi* bacteria. The immunogenicity of TYPHERIX has been established in a randomised active controlled clinical trial comparing TYPHERIX with another Vi polysaccharide typhoid vaccine in over 370 adult participants. Seroconversion rates and geometric mean anti Vi antibody titres were comparable for the two vaccines over the period of the trial. At least 96% of participants had seroconverted (seroconversion was defined as an increase in anti-Vi antibody titres from < 150EL.U/mL pre vaccination to ≥ 150EL.U/mL post vaccination) two weeks after vaccination, with GMTs of >1550 EL.U/ml. The immunogenicity of TYPHERIX in adolescents and children has also been established in three randomised clinical trials comparing TYPHERIX with a typhoid vaccine comparator in 425 children and adolescents (2 - 18 years). One month after vaccination the GMT in children aged 11-18 yrs was 1966 EL.U/ml, in children aged 5-15 yrs the GMT was 2578 EL.U/ml and in children aged 2-5 yrs the GMT was 3597 EL.U/ml. At this time point, seroconversion rates were 98.9%, 99.5%, and 99.3% respectively.

Seropositivity rates (%) and GMT (EL.U/mL) after vaccination of adults with TYPHERIX

		TYPHERIX	Comparator Vi polysaccharide typhoid vaccine
2 weeks	% S^+	96.5	96.8
	GMT	1554	1656
	(n)	(284)	(94)
6 months	% S^+	88.1	84.7
	GMT	700	688
	(n)	(277)	(85)
12 months	% S^+	73.9	66.7
	GMT	380	398
	(n)	(272)	(84)
24 months	% S^+	61.4	45.9
	GMT	290	235
	(n)	(132)	(37)

S^+ = Seropositive

Persistence of Serum Antibodies

Studies to determine persistence of antibody have shown that over 3 years, persistence after a single dose of TYPHERIX is comparable to that of a comparator Vi polysaccharide typhoid vaccine. For participants who returned for blood sampling, over 53% (n=15) of participants remained seropositive at 36 months after vaccination with TYPHERIX compared with 63.6% (n=11) of participants vaccinated with the comparator. Similar geometric mean titers were obtained in both groups (173 and 178 EL.U/ml respectively). Antibody persistence has not been studied in children.

The protective efficacy of TYPHERIX has not been established in humans. As the immunogenicity of TYPHERIX is comparable to that of another Vi polysaccharide typhoid vaccine, efficacy is expected to also be comparable to the comparator vaccine ie. protection in 60-80% of vaccinees during the first year and in 50-77% during the next 2 years.

The simultaneous administration of TYPHERIX with HAVRIX® 1440 was evaluated in randomised trials involving over 460 adults. One month following vaccination, at least 94% of participants in each group were seropositive for anti-Vi antibodies, with GMTs ranging

between 1247 -1331 EL.U./ml. Similar immunogenicity results were observed to those reported following administration of either monovalent vaccine.

Seroconversion (SC) rates and GMT (EL.U/ml) 1 month following administration of TYPHERIX with HAVRIX® 1440 in over 460 adults

	TYPHERIX	HAVRIX® 1440 + TYPHERIX		HAVRIX® 1440
Anti-Vi GMT	1307	1247	1331	-
% SC (n)	94.4 (90)	95.5 (89)	100 (44)	
Anti-HAV GMT	-	367	517	462
% SC (n)		98.0 (49)	97.9 (96)	100 (97)

Note: HAVRIX® 1440+ TYPHERIX = simultaneous administration in opposite arms. The results are from two different studies.

INDICATIONS

TYPHERIX is indicated for active immunisation against typhoid fever for adults and children two years of age and older.

CONTRAINDICATIONS

TYPHERIX should not be administered to participants with known hypersensitivity to any component of the vaccine or to participants having shown signs of hypersensitivity after previous administration.

As with other vaccines, the administration of TYPHERIX should be postponed in participants suffering from acute severe febrile illness. However, the presence of minor infection does not contraindicate vaccination.

PRECAUTIONS

TYPHERIX should under no circumstances be administered intravenously.

It is good clinical practice that immunisation should be preceded by a review of the medical history (especially with regard to previous immunisation and possible occurrence of undesirable events) and a clinical examination.

TYPHERIX protects against typhoid fever caused by *Salmonella typhi*. Protection is not conferred against paratyphoid fever or illness caused by non-invasive Salmonellae. The importance of scrupulous attention to personal, food and water hygiene must be emphasised for all persons at risk of typhoid fever.

As with all injectable vaccines, appropriate medical treatment (ie. adrenaline) and supervision should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

TYPHERIX should be administered with caution to participants with thrombocytopenia or bleeding disorders since bleeding may occur following an intramuscular administration to these participants : following injection, firm pressure should be applied to the site (without rubbing) for at least two minutes. In persons with immunodeficiency, the expected immune response after vaccination with TYPHERIX may not be observed.

As with other vaccines, vaccination may not be expected to protect 100% of susceptible individuals.

Use in Pregnancy (Category B2)

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available.
However, as with other purified polysaccharide vaccines, one does not expect harm for the foetus. TYPHERIX should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the foetus.

Use in Lactation

Adequate human data on use during lactation and adequate animal reproduction studies are not available.
No contra-indication has been established.

INTERACTIONS WITH OTHER MEDICINES

As with other vaccines, it may be expected that patients receiving immunosuppressive treatment or patients with immunodeficiency may not achieve an adequate immune response.

TYPHERIX has been administered simultaneously with HAVRIX® 1440 (inactivated hepatitis A vaccine). The combination was well tolerated with no adverse impact on either reactogenicity or immunogenicity of either vaccine when administered simultaneously.

The concomitant administration of TYPHERIX with vaccines other than HAVRIX® 1440 has not specifically been studied. However, no interaction is anticipated when vaccines are given at separate sites using separate syringes.

ADVERSE EFFECTS

Clinical Trial Experience

In clinical studies, local reactions (redness, pain and swelling) were usually reported during the first 48 hours following immunisation. The most common reaction was pain, reported in approximately 7% of vaccinees. Systemic reactions were also transient. The incidence of the most frequently reported symptoms; fever and headache, did not exceed 9%.

Incidence (%) of solicited local and general symptoms reported in adults

Adverse Event	**TYPHERIX** (n=300)	**Comparator Vi polysaccharide typhoid Vaccine** (n=100)
Soreness	8.3%	33.0
Redness	3.0	21.0
Swelling	2.0	17.0
Fever	2.0	0.0
Headache	7.3	6.0
General aches	1.3	3.0
Malaise	1.0	2.0
Nausea	4.3	2.0
Itching	2.0	1.0

Incidence (%) of solicited local and general symptoms reported in adults, adolescents and children

Adverse Event	Adults	Children & Adolescents
(n)	*551*	*468*
Soreness	9.4%	3.6
Redness	5.4	2.4
Swelling	1.8	1.7
(n)	*400*	*468*
Fever	1.5	16.2
Headache	7.8	10.0
General aches	1.3	4.3
Malaise	4.0	0.9
Nausea	5.0	2.1
Itching	1.8	1.7

Post-Marketing Data

Post-marketing experience with TYPHERIX is currently limited.

Anaphylaxis, allergic reactions, including anaphylactoid reactions and urticaria have been reported very rarely with Typherix.

DOSAGE AND ADMINISTRATION

All parenteral drugs and vaccine products should be inspected visually prior to administration for discolouration or particulate matter. In the event of either being observed, discard the vaccine. Shake well before using TYPHERIX.

Dosage

A single 0.5 ml dose of TYPHERIX is used for immunisation of both children and adults.

Administration

TYPHERIX is administered by intramuscular injection. TYPHERIX SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY. TYPHERIX should be injected intramuscularly into the deltoid region.

Data from 30 healthy adult participants vaccinated with Typherix or a comparator vaccine and followed for 36 months suggests persistence of the immune response. Revaccination every three years is recommended for participants who remain at risk of typhoid fever, although the optimal revaccination schedule has not been established from results of protective efficacy studies.

TYPHERIX should be administered at least 14 days prior to potential exposure to infection with *Salmonella typhi.*

PRESENTATION AND STORAGE CONDITIONS

TYPHERIX should be refrigerated at +2°C to +8°C. **DO NOT FREEZE;** freezing destroys the potency of the product. Discard if vaccine has been frozen.

The expiry date of the vaccine is indicated on the label and packaging. The shelf-life of TYPHERIX is 36 months from the date of manufacture when stored at a temperature of +2°C to +8°C.

TYPHERIX is available in pre-filled syringes, in packs of one or ten.

Pre-filled syringes are made of neutral glass type I, and conform with European Pharmacopoeia Requirements.

MANUFACTURER:

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NAME AND ADDRESS OF THE SPONSOR

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DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG): June 21 1999

DATE OF MOST RECENT AMENDMENT: 6 May 2016

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