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TYPHERIX

1. NAME OF THE MEDICINAL PRODUCT

Typherix, solution for injection in a pre-filled syringe
Typhoid Polysaccharide vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml dose of vaccine contains:

Vi polysaccharide of *Salmonella typhi* (Ty2 strain) 25 micrograms

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in a pre-filled syringe.
Clear isotonic colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

A single dose of 0.5 ml is recommended for both adults and children two years of age and older.

The vaccine should be administered at least two weeks prior to risk of exposure to typhoid fever.

Subjects who remain at risk of typhoid fever should be revaccinated using a single dose of vaccine with an interval of not more than 3 years.

Method of administration

Typherix is for **intramuscular** injection.

Typherix should under no circumstances be administered intravascularly.

4.3 Contraindications

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

As with other vaccines, the administration of Typherix should be postponed in subjects suffering from acute febrile illness. The presence of a minor infection, however, is not a contraindication for vaccination.

4.4 Special warnings and special precautions for use

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic reaction following administration of the vaccine.

The vaccine protects against typhoid fever caused by *Salmonella typhi*. Protection is not conferred against disease caused by *Salmonella paratyphi* and other non-typhoidal *Salmonellae*.

Typherix has not been evaluated in children under 2 years of age. Polysaccharide vaccines in general have lower immunogenicity under this age.

Different injectable vaccines should always be administered at different injection sites.

Typherix should be administered with caution to subjects with thrombocytopenia or bleeding disorders since bleeding may occur following an intramuscular administration to these subjects: following injection, firm pressure should be applied to the site (without rubbing) for at least two minutes.

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate response may not be achieved.

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.

4.5 Interaction with other medicinal products and other forms of interaction

In clinical studies in adults aged over 18 years, Typherix has been administered concomitantly in opposite arms with Havrix Monodose (1440), GlaxoSmithKline's inactivated hepatitis A vaccine.

There was no adverse impact on either the reactogenicity or immunogenicity of the vaccines when they were administered simultaneously in opposite arms.

No interaction studies with other vaccines have been performed.

4.6 Pregnancy and lactation

Pregnancy

The effect of Typherix on fetal development has not been assessed.

Typherix should only be used during pregnancy when there is a high risk of infection.

Lactation

The effect on breastfed infants of the administration of Typherix to their mothers has not been evaluated.

Typherix should therefore only be used in breastfeeding women when there is a high risk of infection.

4.7 Effects on ability to drive and use machines

Some of the effects mentioned under section 4.8 "Undesirable Effects" may affect the ability to drive or operate machinery.

4.8 Undesirable effects

During clinical studies, the most commonly reported adverse events after the first dose were reactions at the injection site, including soreness, redness and swelling.

Frequencies are reported as:

Common: (≥ 1/100 to < 1/10)

Very rare: (< 1/10,000)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

General reactions that may occur in temporal association with Typherix vaccination include:

Clinical studies

Nervous system disorders:

Common: headache

Gastrointestinal disorders:

Common: nausea

Skin and subcutaneous tissue disorders:

Common: itching

General disorders and administration site conditions:

Common: fever, general aches, malaise

Following a second dose, there was an increased incidence of redness and soreness (>10%).

Local reactions were usually reported during the first 48 hours and systemic reactions were also transient.

Post-marketing

The following reactions have been reported in post-marketing experience:

Skin and subcutaneous tissue disorders:

Very rare: urticaria

Immune system disorders:

Very rare: anaphylaxis, allergic reactions, including anaphylactoid reactions

4.9 Overdose

Occasional reports of overdose have been received. The symptoms reported in these cases are not different from those reported following normal dosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial vaccine, ATC code: J07AP03

In comparative clinical studies, the immune response to Typherix was shown to be equivalent to a licensed comparator Vi polysaccharide vaccine. Seroconversion was observed in >95% of Typherix recipients when measured at two weeks after administration. Two years after vaccination 61% were seropositive, and at three years 46%.

The protective efficacy of Typherix has not been investigated in clinical trials.

For individuals who remain at - or who may be reexposed to - risk of typhoid fever, it is recommended that they be revaccinated using a single dose of vaccine with an interval of not more than 3 years.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines and formal pharmacokinetic studies have not been performed.

5.3 Preclinical safety data

No preclinical safety testing with the vaccine has been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, Sodium dihydrogen phosphate dihydrate, Disodium phosphate dihydrate, Phenol and water for injection.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Special precautions for storage

Store in a refrigerator (2°C-8°C)
Do not freeze.

Store in the original package, in order to protect from light.

6.4. Nature and contents of container

0.5 ml of solution in a pre-filled syringe (Type I glass) with a plunger stopper in pack size of 1.

6.5. Special precautions for disposal and other handling

Vaccines should be inspected for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the vaccine.

Shake before use.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER

GlaxoSmithKline Biologicals SA, Rixensart , Belgium

8. LICENSE HOLDER AND IMPORTER

GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach-Tikva