DATA SHEET

Name of Medicinal Product

HEPATYRIX

Inactivated hepatitis A and purified Vi polysaccharide typhoid vaccine

Presentation

HEPATYRIX™ is a combined vaccine formulated by pooling bulk preparations of the purified, inactivated hepatitis A virus (HM175 hepatitis A virus strain) adsorbed onto aluminium hydroxide and the Vi capsular polysaccharide extracted from *Salmonella typhi* Ty2 strain.

HEPATYRIX™ meets the WHO requirements for manufacture of biological substances and complies with the European Pharmacopoeia monograph for Vi polysaccharide typhoid vaccines and the European Pharmacopoeia monograph for Hepatitis A vaccine (inactivated, adsorbed).

Each 1 ml dose of vaccine contains 25 µg of the Vi polysaccharide of *Salmonella typhi* and not less than 1440 ELISA Units (EL.U.) of inactivated hepatitis A viral antigen.

Therapeutic indications

HEPATYRIX™ is indicated for active immunisation of adults and adolescents older than 15 years of age at risk of both hepatitis A virus infection and typhoid fever.

Immunisation with HEPATYRIX™ is particularly recommended in subjects who are, or will be, at increased risk of infection such as travellers from countries of low endemicity to areas where the prevalence of hepatitis A and typhoid fever is high.

Posology and method of administration

The vaccine is a ready-to-use suspension. It must be shaken well before use, since upon storage, the vaccine settles down as a fine white deposit with a clear colourless supernatant. After shaking the vaccine is a slightly opaque, white suspension. Discard if the contents appear otherwise. All parenteral compounds and vaccine products should be inspected visually prior to administration for discolouration or particulate matter.

Dosage

A dose of 1.0 ml is recommended for adults and adolescents older than 15 years of age.

A single dose of HEPATYRIX™ is used for primary immunisation. For travellers, this dose should be given at least 2 weeks prior to departure.

Booster dose

The anti-HAV and anti-Vi antibody titres observed following primary immunisation with the combined vaccine are in the range of what is seen following vaccination with the monovalent vaccines. General guidelines for booster vaccination can therefore be drawn from experience with the monovalent vaccines.

A booster dose of hepatitis A vaccine (HAVRIX 1440), is recommended at any time between 6 and 12 months after a single dose of HEPATYRIX, in order to ensure long term protection against hepatitis A. Subjects who remain at risk of typhoid fever should be revaccinated using a single dose of the Vi vaccine (TYPHERIX), every 3 years.

HEPATYRIX may also be administered as a booster dose between 6 and 12 months following primary immunisation with HAVRIX 1440.

Method of administration

HEPATYRIX™ is for **intramuscular** administration in the deltoid region.

The vaccine should not be administered in the gluteal region.

HEPATYRIX™ should not be administered subcutaneously/intradermally since administration by these routes may result in a suboptimal response to the vaccine. Only in exceptional circumstances can HEPATYRIX™ be administered subcutaneously to subjects with thrombocytopenia or bleeding disorders since bleeding may occur following an intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

HEPATYRIX™ should under no circumstances be administered intravenously.

Contraindications

HEPATYRIX™ 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 of HEPATYRIX or the monovalent vaccines Typherix™ and Havrix™.

Special warnings and special precautions for use

As with other vaccines, the administration of HEPATYRIX™ should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contra-indication for vaccination.

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.

It is possible that subjects may be in the incubation period of a hepatitis A infection at the time of vaccination. It is not known whether HEPATYRIX™ will prevent hepatitis A in such cases.

HEPATYRIX™ will not prevent hepatitis infection caused by other agents such as hepatitis B virus, hepatitis C virus, hepatitis E virus or other pathogens known to infect the liver.

HEPATYRIX™ protects against typhoid fever caused by *Salmonella typhi*. Protection is not conferred against paratyphoid fever or illness caused by non-invasive Salmonellae.

HEPATYRIX™ contains traces of neomycin. The vaccine should be used with caution in patients with known hypersensitivity to one of these antibiotics.

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

HIV infection is not considered as a contra-indication for vaccination with HEPATYRIX™. In subjects with an impaired immune system, adequate anti-HAV and anti-Vi antibody titres may not be obtained after a single dose of HEPATYRIX™ and such patients may therefore require administration of additional doses of vaccine.

Interaction with other medicaments and other forms of interaction

HEPATYRIX™ contains purified inactivated hepatitis A antigen and purified Vi capsular polysaccharide. Therefore, although concomitant use with other inactivated vaccines has not specifically been studied, it is anticipated that no interaction will be observed.

When concomitant administration of other vaccines is considered necessary, different syringes and different injection sites must be used.

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

Pregnancy and lactation

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available. However, as with all inactivated viral vaccines and purified polysaccharide vaccines, the risks to the foetus are considered to be negligible.

HEPATYRIX™ should be used during pregnancy only when there is a clear risk of hepatitis A and typhoid fever.

Adequate human data on use during lactation and adequate animal reproduction studies are not available.

Although the risk can be considered as negligible, HEPATYRIX™ should be used in breastfeeding women only when there is a high risk of infection.

Effects on ability to drive and use machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

Undesirable effects

In controlled clinical studies, the most commonly reported reactions were those at the site of injection. They included pain (66.1%, 8.4% reported as severe), erythema (14.4%, 0.3% severe) and swelling (6.1%, 0.1% severe). All local symptoms resolved without any sequelae.

Systemic adverse events, considered to be probably related or suspected to be related to vaccination, commonly reported in subjects older than 15 years of age were malaise (9.2%, 0.3% severe), headache (8.9%, 0.1% severe), general aches (8.5%, 0% severe), nausea (2.3%, 0.1% severe), itching (1.8%, 0% severe) and fever (1.1%, 0% severe).

All unsolicited symptoms, considered to be probably related or suspected to be related to vaccination, were uncommonly reported.

In controlled clinical studies conducted with the monovalent hepatitis A vaccine, systemic adverse events such as vomiting and loss of appetite were also reported.

Cases of fatigue, diarrhoea, myalgia, arthralgia, allergic reactions including anaphylactic reactions, and convulsions have been reported very rarely following administration of Havrix, the hepatitis A component of Hepatyrix.

Extremely rarely allergic reactions, including anaphylactoid reactions, have been reported following administration of Typherix, the typhoid component of Hepatyrix.

Overdose

Not applicable.

Pharmacological properties

Pharmacodynamic properties

HEPATYRIX™ confers immunity against typhoid fever and HAV infection by inducing specific anti-Vi and anti- HAV antibodies.

In clinical studies involving subjects of 15-50 years of age, seropositivity rates for anti-HAV and anti-Vi antibodies were 89.8% and 97.5% respectively two weeks after primary immunisation. At month 1, seropositivity rates for anti-HAV and anti-Vi antibodies were 99.0% and 95.8% respectively.

Persistence of Serum Antibodies

A study to determine persistence of antibody with HEPATYRIX has shown that over 53% (n = 113) of subjects remained seropositive for anti-Vi antibodies at 36 months after vaccination with HEPATYRIX. All subjects (n = 115) remained seropositive for anti-HAV antibodies 36 months after primary vaccination with HEPATYRIX. A booster of HAVRIX 1440 was administered at six months following primary vaccination with HEPATYRIX.

Hepatitis A component :
According to data available 8 years after primary vaccination with the monovalent hepatitis A vaccine, anti-HAV antibodies are predicted to persist for at least 20 years after a booster dose of HAVRIX 1440 between 6 and 12 months following administration of HEPATYRIX.

Salmonella typhi Vi component :
Based on experience with the monovalent vaccine TYPHERIX, it is expected that immunity persists for at least 3 years after vaccination with HEPATYRIX.

Therefore, due to different booster requirements, monovalent vaccines are recommended to boost immunity against typhoid fever and HAV infection following primary immunisation with HEPATYRIX.

Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

Preclinical safety data

Not applicable.

Pharmaceutical particulars

List of excipients

Aluminium hydroxide, sodium chloride and water for injections. Formaldehyde, polysorbate 20, amino acids for injection, trometamol, and neomycin are present as residuals from the manufacturing process.

Incompatibilities

HEPATYRIX should not be mixed with other vaccines in the same syringe.

Special precautions for storage

HEPATYRIX should be stored at +2°C to +8°C. Protect from light.

Do not freeze; discard if vaccine has been frozen.

During transport, recommended conditions of storage should be respected.

Shelf life

The expiry date of the vaccine is indicated on the label and packaging. The shelf life of HEPATYRIX syringe presentation is 24 months from the date of manufacture at a temperature of +2°C to +8°C and for HEPATYRIX vial presentation is 24 months from the date of manufacture at a temperature of +2°C to +8°C.

Medicine Classification

Prescription Medicine.

Package Quantities

Prefilled syringes in packs of 1 or 10.
Vials in packs of 1 or 10.

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