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STAMARIL PI TGA approved 09/04/98 MA 23/07/98 ~~SRC 27/03/03~~

# PRODUCT INFORMATION
# STAMARIL®
# [YELLOW FEVER VACCINE (LIVE), STABILISED]

## NAME OF PREPARATION

Yellow Fever Vaccine (Live), Stabilised

## DESCRIPTION

Each 0.5mL dose of reconstituted vaccine from the freeze-dried product contains an injectable suspension in stabiliser of the attenuated 17 D strain of yellow fever virus. The virus has been propagated in specific pathogen-free chick embryos, in particular free from avian leucosis viruses. Each dose contains not less than 1000 mouse $LD_{50}$ units.

Other ingredients;

| | |
|---|---|
| Stabilising medium: | 16.0 mg lactose, 8.0 mg sorbitol, 833 µg L-histidine hydrochloride, 362 µg L-alanine, 1.6 mg sodium chloride, 54 µg potassium chloride, 598µg sodium phosphate-dibasic dodecahydrate, 63 µg potassium phosphate-monobasic, 39 µg calcium chloride, 29µg magnesium sulfate. |
| Diluent: | 0.4% sodium chloride solution. |

STAMARIL® has been manufactured in a facility approved by the World Health Organization.

The manufacture of this product includes exposure to bovine 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.

## PHARMACOLOGY

STAMARIL® is a live stabilised vaccine for active immunisation against yellow fever. Immunity appears 7 to 10 days after injection and lasts at least 10 years.

## INDICATIONS

Prevention of yellow fever. Vaccination is recommended for:

- Every person over 6 months of age living or travelling through an endemic area.
- Non-vaccinated persons moving from an endemic to a potentially receptive non-endemic area.

- Laboratory workers handling potentially infected materials.

- In order to be officially recognised, the yellow fever vaccination must be administered in an approved vaccination centre and registered on an international certificate. This certificate is valid from the 10th day after vaccination for 10 years.

## CONTRAINDICATIONS

Pregnancy constitutes a contraindication considering the data available at the present time. However, a vaccination carried out during an unsuspected pregnancy, even during the first trimester, does not justify a termination of pregnancy. In case of outbreaks, the vaccine may be administered in pregnant women after the assessment of the risk related to the epidemiological context.

Not for use in children under 6 months of age.

Allergy to any components of the vaccine, especially eggs and egg protein (including ovalbumin) or severe reaction after previous administration of the vaccine.

Vaccination should be postponed in the case of fever, acute illness or chronic disease in evolution.

STAMARIL® should not be administered to the following individuals:

- patients receiving high-dose oral or injectable corticosteroids or other immunosuppressive treatment, including radiation therapy;

- those suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticuloendothelial system, including those in remission who have received chemotherapy within the last 6 months;

- patients with impaired immunological mechanisms, such as severe combined immunodeficiency, symptomatic HIV-positive individuals or patients with CD4 count less than 200/mm$^3$, and patients who have had recent bone marrow or other organ transplants.

## PRECAUTIONS

Only for intramuscular or subcutaneous injection. Do not inject by intravascular route.

As with other injectable vaccines, appropriate medical treatment and supervision should always be available in cases of anaphylactic reactions. Adrenaline should always be readily available whenever the injection is given.

Provided adequate provision is made for observation and any needed treatment of the patient, individuals with suspected allergy to the vaccine may have a skin test of 0.1mL of vaccine intradermally. If there has been no reaction within 15 minutes, the remainder of the dose (ie. 0.4mL) can be given subcutaneously.

Care should be taken in administering the vaccine to children under 12 months because of theoretical risk of encephalitis.

In children born to HIV positive mothers: the inevitable passage of maternal IgG antibodies through the placenta makes the child's serology uninterpretable until the age of about 9-10 months. NOTE: the persistence of circulating antibodies of maternal origin has been detected at up to 14 months of age. If is therefore necessary to obtain confirmation of the child's HIV status, determined by immunotransfer (Western Blot), possibly using viral genome detection techniques:

- If the child is not infected with HIV: STAMARIL® can be administered as routinely advised.
- If the child is infected with HIV: the advice of specialist paediatric team must be sought.

As yellow fever vaccine-associated viscerotropic disease has been reported to occur within a few days of vaccination, it is advised to monitor adverse events for 10 days post-vaccination.

Thymic disease has been identified as potentially influencing the development of yellow fever vaccine-associated viscerotropic disease (see Adverse Reactions). Health care providers are advised to ask for a history of thymus disorder, including myasthenia gravis, thymoma or prior thymectomy, prior to administering yellow fever vaccine. Alternatives means of prevention in such patients must be considered.

An analysis carried out by the US Centres for Disease Control and Prevention, studied yellow fever vaccine adverse events from 1990 to 1998. This demonstrated an increased frequency of reported serious adverse events (neurologic or systemic reactions persisting more than 48 hours) in patients 65 years of age and older, as compared to other age groups.

Therefore, the health status of individuals 65 years of age or older travelling to areas experiencing ongoing epidemic yellow fever should be evaluated prior to vaccination. These individuals should be carefully monitored for adverse events for 10 days post-vaccination (see Adverse Reactions). The risk of a rare reaction to Yellow Fever vaccine in these elderly travellers must be balanced against their risk of yellow fever infection. It is important to assess the need for vaccination based on the epidemiology of yellow fever in the proposed travel area.

**Use in Pregnancy Category B2**

As with all live vaccines, pregnancy constitutes a contraindication, particularly during the first trimester. However a vaccination carried out during an unsuspected pregnancy does not justify termination of pregnancy. In the case of outbreaks, the vaccine may be administered in pregnant women after assessment of the risk related to the epidemiological context.

**Use in Lactation**

No data exists on the use of STAMARIL® during lactation. There is a theoretical risk of transmission of the live attenuated Yellow Fever virus in STAMARIL® from vaccinated breastfeeding mothers to the newborn. This applies particularly when the newborn is below 4 months of age.

**Interactions With Other Drugs**

To avoid reduction in serological responses:

- Another live vaccine, if not given concurrently with STAMARIL®, should be given after four weeks have elapsed.
- The administration of either injectable cholera vaccine or whole cell paratyphoid or typhoid vaccines concomitantly with STAMARIL® is not recommended. A period of 4 weeks is recommended between yellow fever vaccination and these other vaccinations.

Available data supports concomitant use of STAMARIL® with polysaccharide typhoid vaccine in separate syringes at separate sites. Data concerning other vaccines is limited. However, no interaction is anticipated when vaccines are given at separate sites using separate syringes.

**ADVERSE REACTIONS**

The data used to calculate the rates of common and uncommon adverse reactions have been derived from clinical trials, whereas the rare and very rare adverse reactions are derived from spontaneous reporting of adverse events. The reactions are listed within body systems and categorised by frequency according to the following definitions:

| | |
|---|---|
| Common: | <1/10 and ≥1/100 patients |
| Uncommon: | <1/100 and ≥1/1000 patients |
| Rare: | <1/1000 and ≥1/10000 patients |
| Very rare: | <1/10000 |

**Application Site Disorder**

Common: redness, induration, pain, haematoma

**Body As A Whole**

Common: asthenia, fever
Uncommon: malaise, influenza-like symptoms
Rare: fatigue
Very rare: anaphylactoid reaction, ~~fatigue~~

**Central and Peripheral Nervous System Disorders**

Common: headache
Rare: meningitis, encephalitis
Very rare: meningo-encephalitis, ~~meningitis,~~ severe headache, neuritis, Guillain-Barré Syndrome

**Gastro-intestinal System Disorders**

Uncommon: nausea, vomiting, diarrhoea

**Musculo-skeletal System Disorder**

Common: myalgia
Rare: arthralgia, abdominal pain, arthritis

**Skin and Appendage Disorders**

Rare: rash, urticaria
Very rare: eczema, ~~urtic~~aria, oedema

**Haematological**

~~Very r~~Rare: lymphadenopathy (associated with the injection site)

**Liver and Biliary System disorders**

Very rare: liver dysfunction, varying in severity from mild to severe

Cases of meningitis or meningo-encephalitis have been reported, with an incidence of 1 in a million or less, and a causal relationship has not been clearly demonstrated. Between the fourth and seventh day post-vaccination a reaction may occur taking the form of fever and generalised muscle and/or neck stiffness, accompanied by tiredness and headache.

~~Exceptionally, cases of multi-organ system failure (with death as an outcome) have been reported following vaccination with the 17D strain of yellow fever virus vaccine, with the first symptoms occurring within a few days after vaccination. The pathophysiological mechanism of such a reaction has not been determined (See Precautions).~~
Very rarely, viscerotropic illness (formally described as multi-organ system failure) has been reported following vaccination with STAMARIL® and also following yellow fever vaccination from other manufacturers. The symptom onset was 2-5 days after the vaccination. Initial symptoms are non-specific and they include pyrexia, myalgia, and headache leading quickly to liver and muscle cytolysis and possibly to thrombocytopenia, lymphopenia and acute renal failure. The pathophysiological mechanism of such reaction has not been determined. Whether and in what way underlying genetic or acquired host factors, pre-existing clinical conditions and concomitant drugs might have contributed to the course of viscerotropic illness is unknown.

## DOSAGE AND ADMINISTRATION

A single 0.5-mL dose given by intramuscular or subcutaneous injection provides protection for at least 10 years.

The vaccination schedule is identical for adults and children over 6 months.

The contents of each ampoule should be carefully rehydrated with the accompanying syringe diluent. After complete dispersion, the vaccine is withdrawn back into the syringe and is ready for injection. Strict aseptic technique should be employed when rehydrating and withdrawing the reconstituted product back into the syringe. The reconstituted vaccine should be used as soon as possible and must be used within one hour of reconstitution.

## PRESENTATION AND STORAGE

1 single dose lyophilised vaccine vial + (0.5mL) diluent syringe.

Store at 2-8°C. Do not freeze. Protect from light.

## MANUFACTURED BY

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