AUSTRALIAN PRODUCT INFORMATION

NAME OF THE MEDICINE

STAMARIL®
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 17D 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 IU.

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, 298μg sodium phosphate-dibasic dihydrate, 63 μg potassium phosphate-monobasic, 39 μg calcium chloride, 29 μg magnesium sulfate.
Diluent:	0.4% sodium chloride solution.

STAMARIL is a beige to orange beige powder, which after reconstitution with sodium chloride solution forms a beige to pinked beige suspension, more or less opalescent.

STAMARIL meets the World Health Organization (WHO) requirements for manufacture of biological substances.

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 9 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 10^{th} day after vaccination for 10 years.

CONTRAINDICATIONS

Known systemic hypersensitivity reaction to eggs or chicken proteins or any component of STAMARIL or after previous administration of the vaccine or a vaccine containing the same components.

Vaccination must be postponed in case of febrile or acute disease.

Pregnancy constitutes a contraindication considering the data available at the present time. STAMARIL should be given to pregnant women only when clearly needed, and following an assessment of the risks and benefits.

Children under 6 months of age should in no instance receive yellow fever vaccine due to the risk of encephalitis.

Congenital or acquired immune deficiency impairing cellular immunity, including immunosuppressive therapies such as chemotherapy, high doses of systemic corticosteroids given generally for 14 days or more.

Symptomatic HIV-infected persons.

HIV-infected persons who are asymptomatic and who have established laboratory verification of non-adequate immune system function as per specialist assessment and local recommendations.

History of thymus disorder (including *myasthenia gravis*, thymoma or prior thymectomy). Thymic disease has been identified as potentially influencing the development of yellow fever vaccine-associated viscerotropic disease. Healthcare providers are advised to ask for a history of thymus disorder (including *myasthenia*

gravis, thymoma or prior thymectomy) prior to administering yellow fever vaccine. Alternative means of prevention in such persons is to be considered.

PRECAUTIONS

It is important to evaluate whether the person to be vaccinated plans to live in or travel to or travel through a yellow fever endemic or epidemic country or area. It is also important to evaluate whether the person may have pre-disposing risk factors (see below).

- **Yellow fever vaccine associated neurotropic disease**

Very rarely, yellow fever vaccine-associated neurotropic disease (YEL-AND) has been reported following vaccination, with sequelae or with fatal outcome in some cases (refer to ADVERSE EFFECTS). Clinical features have appeared within one month of vaccination and include high fever with headache that may progress to include one or more of the following: confusion, encephalitis/encephalopathy, meningitis, focal neurological deficits, or Guillain Barré syndrome. To date, those affected have been primary vaccinees. The risk appears to be higher in those aged over 60 years, and below 9 months of age (including transmission from nursing mothers to the infants) although cases have been also reported in other age groups.

- **Yellow fever vaccine-associated viscerotropic disease**

Very rarely, yellow fever vaccine-associated viscerotropic disease (YEL-AVD) resembling fulminant infection by wild-type virus has been reported following vaccination (refer to ADVERSE EFFECTS). The clinical presentation may include fever, fatigue, myalgia, headache, hypotension, progressing to one or more of metabolic acidosis, muscle and liver cytolysis, lymphocytopenia and thrombocytopenia, renal failure and respiratory failure. The mortality rate has been around 60%. To date, cases of YEL-AVD have been in primary vaccinees with onset within 10 days of vaccination. The risk appears to be higher in those aged over 60 years although cases have been reported also for younger persons. Disease of the thymus gland has also been recognised as a potential risk factor.

- **Immune status of the person**

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. It 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.

Persons under immunosuppressive treatments
For persons following an immunosuppressive treatment, it is recommended to delay the vaccination until the immune function has recovered.

In persons taking high doses of systemic corticosteroids given for 14 days or more, it is advisable to wait for at least one month.

Persons following other immunosuppressive treatments should seek advice from a specialist.

HIV infection
STAMARIL must not be administered to persons with symptomatic HIV infection or with asymptomatic HIV infection when accompanied by evidence of impaired immune function. However, there are insufficient data at present to determine the immunological parameters that might differentiate persons who could be safely vaccinated and who might mount a protective immune response from those in whom vaccination could be both hazardous and ineffective. Therefore, if an asymptomatic HIV-infected person cannot avoid travel to an endemic area available official guidance should be taken into account when considering the potential risks and benefits of vaccination.

- **Age**

Children aged 6 to 9 months
Routinely, only children aged 9 months and above should be vaccinated. However, during outbreak control when mass vaccination campaigns are needed in order to interrupt the circulation of yellow fever virus, vaccination of children aged 6 to 9 months could be considered.

Persons aged 60 years and older
Analysis of yellow fever vaccines adverse events demonstrated an increased frequency of serious adverse events (systemic or neurologic reaction persisting more than 48 hours), including YEL-AVD and YEL-AND, in persons 60 years of age and older when compared to other age groups. In this population, the risk of a rare reaction to yellow fever vaccine must be balanced against the risk of yellow fever infection.

Persons with rare hereditary problems of fructose intolerance should not take this vaccine.

As with any vaccine, vaccination with STAMARIL may not protect 100% of vaccinated persons.

Administration
Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.

Because intramuscular injection can cause injection site haematoma, STAMARIL should not be given to persons with any bleeding disorder, such as haemophilia or thrombocytopenia, or to persons on anticoagulant therapy unless the potential benefits clearly outweighs the risk of administration. If the decision is made to administer STAMARIL in such persons, the subcutaneous route should be considered as an alternative to the intramuscular route, and given with steps taken to avoid the risk of haematoma formation following injection.

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.

Effects on fertility

STAMARIL has not been evaluated for the effects on fertility.

Use in Pregnancy - Category B2

As with all live attenuated vaccines, pregnancy constitutes a contraindication. No animal reproduction studies have been conducted with STAMARIL. Data from post marketing surveillance and literature are not sufficient to demonstrate whether STAMARIL can adversely affect pregnancy and embryo-fetal development, parturition and postnatal development. The potential risk is unknown.

STAMARIL should be given to pregnant women only when clearly needed, and following an assessment of the risks and benefit.

Use in Lactation

No data exists on the use of STAMARIL® during lactation. As there is a probable risk of transmission of vaccine components to the infants from breast-feeding mothers, STAMARIL should not be given to nursing mothers unless this cannot be avoided. There are very few reports suggesting that transmission of Yellow Fever vaccine virus may occur from nursing mothers, who received Yellow Fever vaccine postpartum, to the infants. Following transmission the infants may develop yellow fever vaccine associated neurotropic disease (YEL-AND) from which the infants recover.

Paediatric use

Refer to PREACAUTIONS – Age: Children aged 6 to 9 months.

Use in the elderly

Refer to PREACAUTIONS – Age: Persons aged 60 years and older.

Genotoxicity

STAMARIL has not been evaluated for the genotoxic potential.

Carcinogenicity

STAMARIL has not been evaluated for the carcinogenic potential.

Effects on Laboratory Tests

Interference of STAMARIL with laboratory tests has not been studied.

INTERACTIONS WITH OTHER MEDICINES

To avoid reduction in serological responses, another live vaccine, if not given concurrently with STAMARIL, should be given after four weeks have elapsed.

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 EFFECTS

The reactions are listed within body systems and categorised by frequency according to the following definitions:

Very common: ≥ 1/10 (≥ 10%)
Common: < 1/10 and ≥ 1/100 (< 10% and ≥ 1%)
Uncommon: < 1/100 and ≥ 1/1000 (< 1% and ≥ 0.1%)
Rare: < 1/1000 and ≥ 1/10000 (< 0.1% and ≥ 0.01%)
Very rare: < 1/10000, including isolated reports (< 0.01%, including isolated reports)

Clinical Trial Experience

In clinical studies, the most common adverse events occurring after vaccine administration were local reactions, reported in 16% of persons.

General disorders and administration site conditions

Very common: local reactions (including pain, redness, haematoma, induration, swelling)
Common: pyrexia, asthenia

Nervous system disorders

Very common: headache

Gastro-intestinal system disorders

Common: nausea, diarrhoea, vomiting
Uncommon: abdominal pain

Musculo-skeletal and connective tissue disorders

Common: myalgia
Uncommon: arthralgia

Post-Marketing Experience

Based on spontaneous reporting, the following adverse events have been reported following the commercial use of STAMARIL. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship with exposure to STAMARIL.

Skin and subcutaneous tissue disorders

Rash, urticaria

Blood and lymphatic system disorders

Lymphadenopathy
Transient leucopenia

Immune system disorders

Anaphylactoid reaction including angioedemas

Nervous system disorders

Neurotropic disease, described as Yellow Fever Vaccine-Associated Neurotropic Disease (YEL-AND), sometimes fatal, has been reported to occur within 30 days following vaccination with STAMARIL, and also with other Yellow Fever vaccines. The clinical presentation has varied, and includes high fever with headache associated with one or more of confusion, lethargy, encephalitis, encephalopathy, and meningitis.
Other neurological signs and symptoms have been reported and include convulsion, Guillain-Barré Syndrome or focal neurological deficit.

General disorders and administration site conditions
Yellow Fever Vaccine-Associated Viscerotropic Disease (YEL-AVD, formerly described as "Febrile Multiple Organ-System Failure").
YEL-AVD, sometimes fatal, has been reported following STAMARIL and also following administration of yellow fever vaccines from other manufacturers. In the majority of cases reported, the onset of signs and symptoms was within 10 days after the vaccination. Initial signs and symptoms are non-specific and may include pyrexia, myalgia, fatigue and headache, potentially progressing quickly to liver and muscle cytolysis, metabolic acidosis and possibly to thrombocytopenia, lymphopenia and acute respiratory and renal failure.

DOSAGE AND ADMINISTRATION

For adults and children over 9 months of age: a single 0.5 mL dose given by intramuscular or subcutaneous injection provides protection for at least 10 years.

Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.

STAMARIL must not be mixed with any other injectable vaccine(s) or medical product(s).

The freeze-dried powder is reconstituted with the accompanying 0.4% sodium chloride diluent contained in the syringe. The vial is shaken and, after complete dissolution, the suspension obtained is withdrawn into a separate syringe for injection.

Before administration, the reconstituted vaccine should be shaken vigorously.

Use immediately after reconstitution.

Product is for single use in one patient only. Discard any residue.

OVERDOSAGE

There are no reports of overdosage.

PRESENTATION AND STORAGE CONDITIONS

Presentation

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

Storage

Store at 2°C to 8°C (Refrigerate. Do not freeze.) Protect from light.

NAME AND ADRESS OF THE SPONSOR

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POISON SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS

06 July 2000

DATE OF MOST RECENT AMENDMENT

20 October 2014