Professional information for AVAXIM 160 U

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

AVAXIM 160 U suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Inactivated Hepatitis A vaccine, (inactivated, adsorbed)

Each immunising dose (0,5 mL) contains:

160 antigen* units of inactivated** Hepatitis A virus (GBM strain)***

* In the absence of an international standardised reference, the antigen content is expressed using an in-house reference

** adsorbed on aluminium hydroxide, hydrated (expressed as aluminium) 0,3 mg

*** produced on MRC-5 human diploid cells.

Excipients with known effect:

Preservatives: Phenoxyethanol – Ethanol (50 % v/v solution)

2-Phenoxyethanol	2,5 µL
Ethanol anhydrous	2,5 µL

Formaldehyde	12,5 µg

Contains phenylalanine, potassium and sodium.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection

Cloudy, whitish suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AVAXIM 160U is indicated for active immunisation against infection caused by hepatitis A virus in adolescents from 16 years of age and in adults. AVAXIM 160U can be used for primary immunisation or booster.

4.2 Posology and method of administration

The recommended dose is 0,5 mL for each injection.

The primary vaccination consists of one dose of vaccine followed by a booster dose 6 to 36 months apart in order to confer long term protection.

Current recommendations do not support the need for further booster vaccinations for immunocompetent individuals after the initial two-dose vaccination course.

The combined purified Vi polysaccharide typhoid and inactivated hepatitis A vaccine may be given as a booster injection 6 to 36 months after primary immunization by hepatitis A vaccine, in subjects over 16 years travelling to areas where hepatitis A and typhoid are endemic disease.

The vaccine may be used as booster 6 to 36 months after a primary immunization performed by the combined purified Vi polysaccharide typhoid and inactivated hepatitis A vaccine for subjects who are travelling to areas where hepatitis A is an endemic disease.

Method of administration

Shake syringe before injection to get a homogeneous suspension.

As AVAXIM 160U is adsorbed, the vaccine must be injected by intramuscular route, in order to minimize local reactions.

The recommended injection site is the deltoid region.

For instructions on preparation of the medicine before administration, see section 6.6.

4.3 Contraindications

- Avaxim 160U should not be administered to anyone with a history of severe allergic reaction to any component of the vaccine (i.e., as defined under section 2) or after previous administration of the vaccine or a vaccine containing the same components or constituents.
- Vaccination must be postponed in case of febrile or acute disease.

4.4 Special warnings and precautions for use

As each dose contains formaldehyde, caution should be exercised when the vaccine is

administered to subjects with hypersensitivity to this product.

As each dose may contain undetectable traces of neomycin, which is used during vaccine production, caution should be exercised when the vaccine is administered to subjects with hypersensitivity to this antibiotic (and other antibiotics of the same class).

AVAXIM 160 U does not provide protection against infection caused by hepatitis B virus, hepatitis C virus, hepatitis E virus, or by other known liver pathogens.

Because of the incubation period of hepatitis A infection may be present but not clinically apparent at the time of vaccination. The effect of AVAXIM 160 U administration in individuals, late in the incubation period of hepatitis A, has not been documented. In such cases, vaccination should not modify the course of infection.

As with any vaccine, vaccination with AVAXIM 160 may not protect 100 % of susceptible individuals.

The immunogenicity of AVAXIM 160 U could be reduced by immunosuppressive treatment or immunodeficiency. In such cases it is recommended to postpone the vaccination until the end of the disease or treatment. Nevertheless, vaccination of subjects with chronic immunodeficiency such as HIV infection is recommended even if the antibody response might be limited.

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

As with all injectable vaccines, the vaccine must be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

In exceptional circumstances, the vaccine may be administered by the subcutaneous route in patients suffering from thrombocytopenia or in patients at risk of hemorrhage.

Prior to administration of any dose of AVAXIM 160U, the parent or guardian of the recipient or the adult recipient himself must be asked about his personal history, family history, and recent health status, including immunization history, current health status, and any adverse event after previous immunizations. In subjects who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, the course of the vaccination must be carefully considered.

Before the injection of any biological product, the person responsible for administration must take all precautions known for the prevention of allergic or any other reactions.

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

As a precautionary measure, epinephrine injection (1:1 000) must be immediately available in case of anaphylactic or serious allergic reactions.

Syncope (fainting) may occur following, or even before any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling injury and manage syncopal reactions.

Avaxim 160U contains ethanol, phenylalanine, potassium and sodium

- This medicine contains small amounts of alcohol (ethanol), less than 100 mg per dose.
- This medicine contains 10 microgram phenylalanine in each 0,5 mL dose which is equivalent to 0,17 microgram/kg for a 60 kg person. Phenylalanine may be harmful for people with phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.
- This medicine contains less than 1 mmol of potassium (39 mg) and sodium (23 mg) per dose, i.e., it is essentially ‘potassium-free’ and ‘sodium-free’.

4.5 Interaction with other medicines and other forms of interaction

Separate injection sites and separate syringes must be used in case of concomitant administration with other medicines.

Concomitant administration of immunoglobulins and AVAXIM 160U at two separate sites may be performed. Seroconversion rates are not modified, but antibody titres could be lower than after vaccination with the vaccine alone. When concomitant administration of other vaccines is considered necessary, the vaccines must be given with different syringes at different injection sites.

AVAXIM 160U may be administered simultaneously, but at separate sites with typhoid polysaccharide vaccine without modification of the immune response to either antigen.

This vaccine may be administered simultaneously, but at separate sites, with a live and stabilized yellow fever vaccine.

AVAXIM 160U can be used as a booster in subjects previously vaccinated with another inactivated hepatitis A vaccine.

Immunogenicity of the vaccine could be impaired by immunosuppressive treatment.

As the vaccine is inactivated, association with other inactivated vaccine(s) given at a different injection site is unlikely to interfere with immune responses.

AVAXIM 160U can be administered simultaneously in two separate injection sites, with a typhoid polysaccharide Vi vaccine, with no modification of immune response to each antigen injected separately.

Concomitant administration of immunoglobulins and AVAXIM 160U at two separate sites may be performed. Seroconversion rates are not modified, but antibody titres could be lower than after vaccination with the vaccine alone.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal reproduction studies have not been conducted with AVAXIM 160U.

Data on the use of this vaccine in pregnant women are limited. Therefore, the administration of AVAXIM 160U during pregnancy is not recommended. AVAXIM 160U should be given to pregnant women only if clearly needed, and following an assessment of the risks and benefit.

Breastfeeding

It is not known whether AVAXIM 160U is excreted in human milk. Caution must be exercised when AVAXIM 160U is administered to a nursing mother.

Fertility

No data on fertility available.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Data from clinical studies

The adverse events reported during clinical trials were generally mild, short term and transient without treatment.

Nervous system disorders

Common: headache

Gastrointestinal disorders

Common: nausea, vomiting, decreased appetite, diarrhoea, abdominal pain

Musculoskeletal and connective tissue disorders

Common: myalgia, arthragia

General disorders and administration site condition

Very common: asthenia, injection site pain

Common: **[**~~M~~**]**mild fever

Uncommon: injection site erythema

Rare: injection site nodule

Investigations

Rare: transaminase increased (mild and reversible)

Reactions were less frequently reported after the booster dose than after the first dose.

In subjects seropositive against hepatitis A virus, AVAXIM 160U is as well tolerated as in seronegative subjects.

The reactions observed in haemophiliac children were identical to those observed in adults.

Data from Post-marketing surveillance

Based on spontaneous reports, the following adverse reactions have been reported following commercial use of AVAXIM 160U. Their frequency is “Not known” (cannot be estimated from available data).

Immune system disorders

Anaphylactic reaction

Nervous system disorders

- Vasovagal syncope, headache

Gastrointestinal disorders

- Nausea, diarrhoea, vomiting, abdominal pain

Skin and subcutaneous tissue disorders

- Urticaria, rashes associated or not with pruritis

Musculoskeletal and connective tissue disorders

- Arthralgia, myalgia

General disorders and administration site condition

- Injection site pain, injection site rash, injection site nodule, pyrexia, asthenia

Investigations

- Transaminase increased (mild and reversible).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256 3700 (tel), or
- SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**" found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Cases of administration of more than the recommended dose (overdose) have been reported with AVAXIM 160U. The adverse events reported in these cases did not differ in nature from those described in section 4.8.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 30.1 Antigens.

Pharmacotherapeutic group: Viral vaccine

ATC code: J07BC02

5.1 Pharmacodynamic properties

This vaccine is prepared from Hepatitis A virus cultured, purified and then inactivated by formaldehyde.

It confers immunity against hepatitis A virus by inducing antibody (anti-HAV) titres greater than those obtained after passive immunization with immunoglobulin.

Immunity (Anti-HAV) appears soon after the first injection, and 14 days after the vaccination, more than 90 % of immunocompetent subjects have anti-HAV above 20 mIU/mL.

One month after the first injection, 100 % of subjects are protected. Anti-HAV persist for at least 36 months and are reinforced after a booster injection.

Data relative to long-term persistence of anti-HAV following vaccination with AVAXIM 160U are not currently available. Nevertheless, available data suggest that anti-HAV persist beyond 10 years after the booster vaccination in healthy individuals.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

2-phenoxyethanol

Aluminium hydroxide, hydrated

Ethanol anhydrous

Formaldehyde

[~~h~~]Hydrochloric acid (pH-adjuster)

Hanks medium 199*

Polysorbate 80

Sodium hydroxide (pH-adjuster)

Water for injections

This vaccine contains undetectable traces of neomycin.

Hanks medium 199 (without phenol red) is a complex mixture of amino acids (including phenylalanine), mineral salts, vitamins and other components.

6.2 Incompatibilities

The vaccine must not be mixed with other vaccines or medicines.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

- Store in a refrigerator (2 °C – 8 °C).
- DO NOT FREEZE. Discard if frozen.
- Store protected from light.

6.5 Nature and contents of container

One 0,5 mL single dose pre-filled syringe (type 1 glass) closed by an elastomer (or chlorobutyl or bromobutyl) plunger stopper with a stainless steel attached needle.

6.6 Special precautions for disposal and other handling

Before injection, shake the syringe well in order to obtain a homogeneous suspension. The vaccine should be visually inspected before
administration for any foreign particulate matter.

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

Hertford Office Park

Building I, 5th Floor, 90 Bekker Road

Vorna Valley, Midrand, 2196

South Africa

8. REGISTRATION NUMBER

30/30.1/0244

9. DATE OF FIRST AUTHORISATION

Date of registration: 01 October 2013

Date of revision: 12 August 2022