SCHEDULING STATUS: **S4**

1. NAME OF THE MEDICINE

AVAXIM 80 suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Hepatitis A vaccine (inactivated, adsorbed)

Each immunising dose (0,5 mL) contains:

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

**adsorbed on aluminium hydroxide (expressed as aluminium) 0,15 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

AVAXIM 80 is a cloudy, whitish suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AVAXIM 80 is indicated for active immunisation against infection caused by hepatitis A virus in children aged 12 months to 15 years inclusive.

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.

Data available on vaccination with AVAXIM 80 show there is no need for further booster vaccinations for immunocompetent individuals after the initial two-dose vaccination course, which is consistent with current recommendations.

In a setting transitioning from high to intermediate endemicity, it was observed that after the administration of a single dose of AVAXIM 80, subjects still show satisfactory anti-HAV response up to 7 years after initial vaccination, which is consistent with WHO recommendations.

Method of administration

Shake syringe before injection to get a homogeneous suspension.

As Avaxim 80 is adsorbed, the vaccine must be injected by intramuscular route in order to minimize local reactions. The recommended sites of injection are: the quadriceps in young children and the deltoid in older children and adolescents.

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

4.3 Contraindications

- AVAXIM 80 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).

The vaccine 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 80 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 80 may not protect 100 % of susceptible individuals.

No study relative to the administration of AVAXIM 80 in patients with impaired immunity has been performed.

The immunogenicity of AVAXIM 80 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 (e.g., patients with thrombocytopenia or in patients at risk of hemorrhage), the vaccine may be injected by the subcutaneous route.

Prior to administration of any dose of AVAXIM 80, 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 immunisation history, current health status, and any adverse event after previous immunisation. 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 a precautionary measure, epinephrine injection (1:1 000) must be immediately available in case of unexpected 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 80 contains ethanol, phenylalanine, potassium and sodium

- This medicine contains 2 mg of alcohol (ethanol) in each 0,5 mL dose. The small amount of amount of alcohol in this medicine will not have any noticeable effects.
- 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.

The vaccine may be administered simultaneously with vaccines containing one or more of the following valences: diphtheria, tetanus, pertussis (acellular or whole cells), *Haemophilus*

influenzae type b, and inactivated or oral poliomyelitis, measles, mumps and rubella.

Concomitant administration of immunoglobulins and AVAXIM 80 can be performed at two separate sites. Seroconversion rates remain unmodified, but antibody titres may be lower than those observed after vaccination with AVAXIM 80 alone.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal reproductive studies have not been conducted with AVAXIM 80. Data on the use of this vaccine in pregnant women are limited. Therefore, the administration of AVAXIM 80 during pregnancy is not recommended. AVAXIM 80 should be given to pregnant women only if clearly needed, and following an assessment of the risks and benefits.

Breastfeeding

It is not known whether AVAXIM 80 is excreted in human milk. Caution must be exercised when AVAXIM 80 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

Within each system organ class the adverse events are ranked under headings of frequency, most frequent reactions first, using the following convention.

Very common: ≥ 1/10 (≥ 10%)

Common: ≥ 1/100, <1/10 (≥ 1% and < 10%)

Uncommon: ≥ 1/1000, <1/100 (≥ 0,1% and < 1%)

Rare: ≥1/10 000, <1/1000 (≥ 0,01% and < 0,1%)

Very rare: <1/10 000 (< 0,01%)

Not known: cannot be estimated from the available data.

Data from clinical studies

More than 6 200 children aged from 12 months to 15 years (around 13 800 administered doses) were vaccinated with AVAXIM 80 during clinical development. A pooled analysis has been performed integrating data from 5458 subjects included in 15 clinical trials conducted between 1996 and 2014.

Metabolism and nutrition disorders

Common: decreased appetite

Psychiatric disorders

Very common: abnormal crying

Common: Irritability, insomnia

Nervous system disorders

Very common: Headache

Gastrointestinal disorders

Common: Abdominal pain, vomiting, diarrhoea, nausea

Skin and subcutaneous tissue disorders

Uncommon: Rash, urticaria

Musculoskeletal and connective tissue disorders

Common: Arthralgia, myalgia

General disorders and administration site condition

Very common: Injection site pain, malaise

Common: Injection site erythema, Injection site induration/edema, pyrexia, asthenia/drowsiness, injection site haematoma.

Most side-effects were confined to the first few days following vaccination with spontaneous recovery. The incidence of severe (grade 3) reactions was low. Reactions were less frequently reported after the booster dose than after the first dose.

In subjects seropositive against hepatitis A virus, AVAXIM 80 is as well tolerated as in seronegative subjects.

Data from Post-marketing experience

Based on spontaneous reporting, the following additional adverse reactions have been reported during the commercial use of Avaxim 80. These reactions have been very rarely (< 0,01 %) reported; however as exact incidence rates cannot be calculated precisely, their frequency is qualified as “Not known”.

Immune system disorders

Anaphylactic reaction

Nervous system disorders

Vasovagal syncope

Convulsions with or without fever

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

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 30.1 Antigens.

Pharmaco-therapeutic group: Viral vaccine

ATC code: J07BC02

5.1 Pharmacodynamic properties

AVAXIM 80 is prepared from hepatitis A virus grown, harvested, purified and formaldehyde inactivated.

The vaccine confers immunity against hepatitis A virus by inducing antibody (anti-HAV) titres longer lasting and higher than those obtained after passive immunisation with immunoglobulins.

This vaccine was demonstrated to elicit protective antibody titres against hepatitis A virus (titre > 20 mIU/mL) within 2 weeks following the injection in over 95 % of individuals and in 100 % of individuals before the booster dose. Anti-HAV titres are reinforced after a booster dose.

After the first dose, anti-HAV antibodies persist for at least 7 years.

Data relative to long-term persistence of anti-HAV antibodies following booster vaccination with

AVAXIM 80 indicate that anti-HAV antibodies persist up to 14-15 years in healthy individuals.

5.2 Pharmacokinetic properties

No pharmacokinetic studies have been performed.

5.3 Preclinical safety data

No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

2-phenoxyethanol

Aluminium hydroxide

Ethanol anhydrous

Formaldehyde

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 without phenol is a complex mixture of amino acids (including phenyalanine), mineral salts (including potassium), vitamins and other components.

6.2 Incompatibilities

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

6.3 Shelf life

Store in a refrigerator (2 °C – 8 °C).

3 years.

6.4 Special precautions for storage

- DO NOT FREEZE. Discard if frozen.
- Store protected from light.
- Use immediately after opening.

6.5 Nature and contents of container

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

6.6 Special precautions for disposal and other handling

Shake before injection 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

8. REGISTRATION NUMBER

35/30.1/0401

9. DATE OF FIRST AUTHORISATION

Date of registration: 04 October 2013

Date of revision: 05 October 2022