

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

AVAXIM, suspension for injection in a pre-filled syringe
Hepatitis A vaccine (inactivated, adsorbed)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One 0.5 millilitre dose contains:

Hepatitis A virus, GBM strain (inactivated)^{1, 2}.....160 U³

¹ produced in human diploid (MRC-5) cells

² adsorbed on aluminium hydroxide, hydrated (0.3 milligrams Al)

³ In the absence of an international standardised reference, the antigen content is expressed using an in-house reference

Excipient(s):

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection in a pre-filled syringe

Hepatitis A vaccine (inactivated, adsorbed) is a cloudy and white suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

AVAXIM is indicated for active immunisation against infection caused by hepatitis A virus in susceptible adults and adolescents of 16 years of age and above.

The use of AVAXIM should be based on official recommendations.

4.2 Posology and method of administration

Posology

The recommended dosage for subjects of at least 16 years of age is 0.5 millilitre for each injection.

Initial protection is achieved with one single dose of vaccine. Protective levels of antibody may not be reached until 14 days after administration of the vaccine.

In order to provide long-term protection, a second dose (booster) of an inactivated hepatitis A vaccine should be given. The second dose is preferably given between 6 and 12 months but may be administered up to 36 months after the first dose (see section 5.1). It is predicted that HAV antibodies persist for many years (beyond 10 years) after the second dose.

The vaccine may be used to provide the second dose (booster) in subjects from 16 years of age who received another inactivated hepatitis A vaccine (monovalent or with purified Vi polysaccharide typhoid) 6 months to up to 36 months previously.

Paediatric population

AVAXIM is not recommended for use in children of less than or equal to 15 years of age due to insufficient data on

safety and efficacy.

Method of administration

AVAXIM should be administered by intramuscular injection in the deltoid region. AVAXIM must not be administered intradermally or intravascularly.

The vaccine should not be administered into the buttocks, due to the varying amount of fatty tissue in this region, contributing to variability in effectiveness of the vaccine.

In exceptional circumstances (e.g. in patients with thrombocytopenia or in patients at risk of haemorrhage), the vaccine may be injected by the subcutaneous route.

Precautions to be taken before handling or administering the medicinal product. For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 or to neomycin, which may be present in the vaccine in trace amounts.
- Hypersensitivity following a previous injection of this vaccine.
- Vaccination should be delayed in subjects with an acute severe febrile illness.

4.4 Special warnings and precautions for use

As with all vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of rare anaphylactic reaction following vaccination. AVAXIM should only be given by a physician or health care worker trained in the administration of vaccines.

Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

AVAXIM has not been studied in patients with impaired immunity. The immune response to AVAXIM could be impaired by immunosuppressive treatment or in immunodeficiency states. In such cases, it is recommended to measure the antibody response to be sure of protection and, if possible, to wait for the end of any suppressive treatment before vaccination. Nevertheless, vaccination of subjects with chronic immunodeficiency such as HIV infection is recommended although the antibody response may be limited.

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 on individuals late in the incubation period of hepatitis A has not been documented.

Individuals having grown up in areas of high endemicity and/or with a history of jaundice may be immune to hepatitis A, in which case the vaccine is unnecessary. Testing for antibodies to hepatitis A prior to a decision on immunisation should be considered in such situations. If not, seropositivity against hepatitis A is not a contraindication. AVAXIM is as well tolerated in seropositive as in seronegative subjects (see Section 4.8).

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

As no studies have been performed with AVAXIM in subjects with liver disease, the use of this vaccine in such subjects should be considered with care.

As with any vaccine, vaccination may not result in a protective response in all susceptible vaccinees.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical data on concomitant administration of AVAXIM with other inactivated vaccine(s) or recombinant hepatitis B virus vaccine have been generated. When concurrent administration is considered necessary, AVAXIM must not be mixed with other vaccines in the same syringe, and other vaccines should be administered at different sites with different syringes and needles.

Seroconversion rates were not modified when AVAXIM was given at the same time as but at a different injection site to a Vi polysaccharide typhoid vaccine or a yellow fever vaccine reconstituted with a Vi polysaccharide typhoid vaccine.

Concomitant administration of immunoglobulin and AVAXIM at two separate sites may be performed. Seroconversion rates are not modified, but antibody titres could be lower than after vaccination with AVAXIM alone. Therefore, consideration should be given to whether or not the subject is likely to be at long-term risk of exposure.

No interaction with other medicinal products is currently known.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of hepatitis A vaccine (inactivated, adsorbed) in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development. The potential risk for humans is unknown.

AVAXIM should not be used during pregnancy unless clearly necessary and following an assessment of the risks and benefits

Breastfeeding

The use of this vaccine is possible during breast-feeding.

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

Adverse event data are derived from clinical trials and worldwide post-marketing experience.

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

Very common ($\geq 1/10$), Common ($\geq 1/100$, $< 1/10$), Uncommon ($\geq 1/1000$, $< 1/100$), Rare ($\geq 1/10000$, $< 1/1000$), Very rare ($< 1/10000$) including isolated reports.

Clinical Studies

In clinical trials, adverse reactions were usually mild and confined to the first few days after vaccination with spontaneous recovery. The adverse reactions observed with AVAXIM were:

Nervous system disorders

Common: headache

Gastrointestinal disorders

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

Musculoskeletal and connective tissue disorders

Common: myalgia/arthritis

General disorders and administration site conditions

Very common: asthenia, mild injection site pain

Common: mild fever

Uncommon: injection site erythema

Rare: injection site nodule

Investigations

Rare: transaminases 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 was as well tolerated as in seronegative subjects.

Post marketing experience

Based on spontaneous reporting, the following additional adverse events have been reported during the commercial use of AVAXIM. These events have been very rarely reported however exact incidence rates are not known (cannot be estimated from the available data).

Nervous system disorders

vasovagal syncope in response to injection

Skin and subcutaneous tissue disorders

urticaria, rashes associated or not with pruritus

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: <http://www.hpra.ie/>; E-mail: medsafety@hpra.ie.

4.9 Overdose

A few cases of overdose have been reported with AVAXIM, without specific adverse event.

5 PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Viral vaccine, ATC Code: J07BC02

AVAXIM confers immunity against hepatitis A virus by inducing antibody titres greater than those obtained after passive immunisation with immunoglobulin. Antibody appears shortly after the first injection and 14 days after vaccination more than 90% of immunocompetent subjects are seroprotected (titre above 20 mIU/millilitre).

One month after the first injection, almost 100% of subjects have antibody titres above 20mIU/millilitre. Serological data show continuing protection against hepatitis A for up to 36 months in subjects who responded to the first dose. In a study of 103 healthy adults who were followed serologically for three years after the first injection of AVAXIM, 99% still had at least 20 mIU/ml anti HAV antibody at month 36.

The long-term persistence of protective antibody levels to hepatitis A virus after a second dose (booster) of AVAXIM has not been fully evaluated. Nevertheless, available data (antibody titres obtained two years after the second dose) suggest that anti-HAV antibodies persist beyond 10 years after the second dose in healthy individuals.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of acute toxicity, repeated dose toxicity, local tolerance and hypersensitivity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

2-phenoxyethanol
Formaldehyde
Medium 199 Hanks *
Water for injections
Hydrochloric acid and sodium hydroxide for pH adjustment

*Medium 199 Hanks is a complex mixture of amino acids (including phenylalanine), mineral salts, vitamins and other components.

6.2 Incompatibilities

In the absence of compatibility studies, the vaccine must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
Do not freeze. If frozen, the vaccine should be discarded.

6.5 Nature and contents of container

0.5 ml of suspension in pre-filled syringe (type I glass) with a plunger-stopper (bromochlorobutyl or chlorobutyl or bromobutyl) and attached needle and needle-shield (natural rubber or polyisoprene).

0.5 ml of suspension in pre-filled syringe (type I glass) with a plunger-stopper (bromochlorobutyl or chlorobutyl or bromobutyl), without needle.

Packs of 1, 5, 10 and 20 syringes.

0.5 ml of suspension in pre-filled syringe (type I glass) with a plunger-stopper (bromochlorobutyl or chlorobutyl or bromobutyl), with 1 or 2 separate needles (for each syringe).

Packs of 1 and 10 syringes.

Not all pack sizes and presentations may be marketed.

6.6 Special precautions for disposal and other handling

For needle free syringes, the needle should be pushed firmly on to the end of the prefilled syringe and rotated through 90 degrees.

Shake before injection to obtain a homogeneous suspension. The vaccine should be visually inspected before administration for any foreign particulate matter.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Sanofi Pasteur Europe
14 Espace Henry Vallée
69007 Lyon
FRANCE

8 MARKETING AUTHORISATION NUMBER

PA2131/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 February 1997

Date of last renewal: 30 April 2006

10 DATE OF REVISION OF THE TEXT

May 2018