AVAXIM 80 U PEDIATRIC

1. NAME OF THE MEDICINAL PRODUCT

AVAXIM 80 U PEDIATRIC, suspension for injection in prefilled syringe
Inactivated Hepatitis A vaccine, adsorbed

AVAXIM 80 U PEDIATRIC, suspension for injection in multidose vial
Inactivated Hepatitis A vaccine, adsorbed

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Hepatitis A virus, GBM strain*, (inactivated)**……80 U***
for one dose of 0.5 mL.

* Cultured on MRC5 human diploid cells
** Adsorbed on hydrated aluminium hydroxide (0.15 milligrams of Al)
*** In the absence of an international standardised reference, the antigen content is expressed using an in-house reference.

For the full list of excipients, see Section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection in prefilled syringe.
Suspension for injection in multidose vial.
The hepatitis A vaccine (inactivated, adsorbed) is a turbid and whitish suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AVAXIM 80 U PEDIATRIC is indicated for active immunization against infection caused by hepatitis A virus in children aged from 12 months to 15 years.

The vaccine should be administered in accordance with official recommendations.

4.2 Posology and method of administration

Posology
Primary vaccination is achieved with one single dose of vaccine. The recommended dosage is 0.5ml for each injection. In order to provide long-term protection, a booster dose is recommended 6 to 36 months following the initial dose.

It is estimated that anti-HAV antibodies persist several years (beyond 10 years) after the second dose (booster).

Method of administration
This vaccine must be administered by the intramuscular route.
The recommended injection site is the deltoid region.

In exceptional cases, the vaccine may be administered by the subcutaneous route in patients suffering from thrombocytopaenia or in patients at risk of haemorrhage.
The vaccine should not be administered into the buttocks because of the varying amount of fat tissue in this region, that may contribute to variability in effectiveness of the vaccine.

Do not inject by the intravascular route: ensure that the needle does not penetrate a blood vessel.

Do not inject by the intradermal route.

4.3 Contra-indications

- Hypersensitivity to the active substance, to one of the excipients, to neomycin (that may be present as traces in each dose due to its use during the manufacturing process).
- Hypersensitivity following a previous injection of this vaccine.
- Vaccination should be postponed in case of severe acute febrile illness.

4.4. Special warnings and special precaution for use

As with all injectable vaccines, available appropriate medical treatment and subject monitoring are recommended in case of an anaphylactic reaction after vaccine administration.

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

AVAXIM 80 U PEDIATRIC has not been studied in patients with impaired immunity.

The immune response to the vaccine may be impaired by immunosuppressive treatment or immunodeficiency. In such cases it is recommended to wait for the end of treatment before vaccinating or to make sure the subject is well protected. Nevertheless, vaccination of subjects with chronic immunodeficiency such as HIV infection is recommended even though the antibody response might be limited.

Because of the incubation period of hepatitis A, infection may already be present, although asymptomatic, at the time of vaccination.

The effect of administering AVAXIM 80 U PEDIATRIC during the incubation period of hepatitis A has not been documented.

In such a case, vaccination may have no effect on the development of hepatitis A.

The use of this vaccine in subjects with liver disease should be considered with caution, as no studies have been performed in such subjects.

As with all vaccines, vaccination may not induce a protective response in some vaccinees.

This vaccine does not protect against infection caused by hepatitis B virus, hepatitis C virus, hepatitis E virus or by other known liver pathogens.

4.5 Interaction with other medicinal products and other forms of interaction

The simultaneous administration of immunoglobulins with this vaccine in two different injection sites may be performed. The seroprotection rates are not modified, but the antibody titres may be lower than those obtained when the vaccine is administered alone.

In case of simultaneous administration, this vaccine must not be mixed with other vaccines in the same syringe. The vaccine may be administered simultaneously, in two different injection sites, with the routine booster vaccine of the child during the second year of life, i.e. various vaccines containing one or more of following valences: diphtheria, tetanus, pertussis (acellular or whole cells), *Haemophilus influenzae* of type b and inactivated or oral poliomyelitis.

This vaccine can be administered simultaneously, but at two different injection sites, with a vaccine against measles, mumps and rubella.

This vaccine can be used as a booster in subjects previously vaccinated with another inactivated Hepatitis A vaccine.

4.6 Pregnancy and lactation

Pregnancy

No relevant teratogenic data on animal are available.

In humans, up to now, the data is inadequate to assess teratogenic or foetotoxic risk of the vaccine against Hepatitis A when administered during pregnancy.

As a precautionary measure, it is preferable not to use this vaccine during pregnancy except in case of a major contamination risk.

Breastfeeding

The excretion of AVAXIM 80U PEDIATRIC in maternal milk is unknown. The excretion of AVAXIM 80U PEDIATRIC in milk has not been studied in animals. The decision to continue/discontinue lactation or whether to administer AVAXIM 80U PEDIATRIC or not should be made taking into account the benefit of breast-feeding for the child and the benefit of AVAXIM 80U PEDIATRIC for the woman.

4.7 Effects on ability to drive and use machines

The effects on the ability to drive and use machines have not been studied.

4.8 Undesirable effects

The undesirable effects are derived from clinical studies and worldwide post-marketing experience.
In each System Organ Class, the undesirable effects are ranked under headings of frequency, the most common reactions coming first, using the following convention:
Very common (≥1/10), Common (≥1/100, <1/10), Uncommon (≥1/1000, <1/100), Rare (≥1/10000, <1/1000), Very rare (<1/10000) including isolated reports.

Clinical studies
More than 3500 children aged from 12 months to 15 years (around 7000 administered doses) were vaccinated with this vaccine during clinical studies.

All undesirable effects were moderate and confined to the first few days following vaccination with spontaneous recovery. Reactions were more rarely reported after the booster dose than after the first dose.

However, as with all pharmaceuticals, expanded commercial use of the vaccine might reveal rarer undesirable effects.

Metabolism and nutrition disorders
Common: appetite decrease.

Psychiatric disorders
Common: irritability, insomnia.

Nervous system disorders
Common: cephalalgia.

Gastrointestinal disorders
Common: abdominal pain, diarrhoea, nausea, vomiting.

Musculoskeletal and connective tissue disorders

Common: arthralgia, myalgia.

General disorders and administration site conditions

Common: local reactions at the injection site such as pain, redness, oedema or induration, fever, asthenia.

Skin and subcutaneous tissue disorders

Uncommon: rash, urticaria.

Post-marketing experience

Based on spontaneous reporting, the following adverse events have also been reported during the commercial use of AVAXIM 80 U PEDIATRIC. These events were very rarely reported. However, the exact incidence is not known (cannot be estimated based on the available data).

Nervous system disorders

Vasovagal syncope in response to injection.

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 the national reporting system.

4.9 Overdose

An overdose is unlikely to provoke any harmful effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Viral vaccine, ATC code: J07BC02

This vaccine is prepared from hepatitis A virus cultured, harvested and then inactivated by formaldehyde.

It confers immunity against hepatitis A virus by inducing antibody titres longer lasting and higher than those obtained after passive immunization with immunoglobulins. This vaccine has been demonstrated to elicit protective antibody titres against the hepatitis A virus (≥20mIU/mL) within two weeks following the injection in over 95% of individuals and in 100% of individuals before the booster dose administration.

Immunity persists for 6 to 36 months and is reinforced after a booster dose.

Long term persistence of a protective level of antibodies to hepatitis A virus after a second dose (booster) of AVAXIM 80 PEDIATRIC has not been currently established. However, the available data suggest that antibodies to hepatitis A virus persist beyond 10 years after the second dose in healthy people.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipient(s)

2-Phenoxyethanol, Formaldehyde and Hanks Medium 199*(without phenol red) supplemented with polysorbate 80.
*Hanks 199 medium is a complex mixture of amino acids (including phenylalanine), mineral salts, vitamins, and other components, diluted in water for injections, with a pH adjusted with hydrochloric acid or sodium hydroxide.

6.2 Incompatibilities
In the absence of compatibility studies, this pharmaceutical product must not be mixed with other medicinal products.

6.3 Shelf-life
3 years

6.4 Special precautions for storage
Single dose presentation
Store between +2°C and +8°C (in a refrigerator) and protected from light. Do not freeze.

Multidose presentation
Store between+2°C and +8°C (in a refrigerator) and protected from light. Do not freeze.
Following opening: an immediate use is recommended.

6.5 Nature and contents of container
Single dose presentation
0.5ml of suspension in prefilled syringe (type I glass) with a plunger-stopper (bromochlorobutyl or chlorobutyl or bromobutyl), with attached needle, without needle or with two separate needles. Box of 1, 10 or 20.

Multidose presentation
5 ml of suspension in vial (type I glass) equipped with a plunger (chlorobutyl)- box of 1 or 10 vials 10 doses.

Not all presentations may be available.

6.6 Instruction for use and handling

Shake before injection, until a homogenous suspension is obtained.

The vaccine must be visually inspected before administration to verify the absence of foreign particles.

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

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR SA
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France.

8. DATE OF REVISION OF TEXT
22 March 2018

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