

مذكرة تقييم الجهة المختصة في مصر
اللهم اكتب في مجلسنا

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

AVAXIM 80 U PEDIATRIC, suspension for injection in pre-filled syringe

Hepatitis A vaccine (inactivated, adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Hepatitis A virus, GBM strain* (inactivated) ** 80 ELISA units***
for one dose of 0.5 mL

* Cultured on MRC-5 human diploid cells

** Adsorbed on hydrated aluminium hydroxide (0.15 milligrams of Al³⁺)

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

Excipient with known effect (see section 4.4):

Phenylalanine 10 micrograms
Per 0.5 mL dose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

The hepatitis A vaccine (inactivated, adsorbed) is a turbid and whitish suspension.

هيئة الدواء المصرية
الادارة المركزية للستحضرات الحيوية والمبتكرة
والدراسات الاعليمية
إدارة تسجيل المستحضرات الحيوية
دورة مناقصات دبلوم حفظ عين العامل
٢٠١٣/٢٠١٤/٢٠١٥/٢٠١٦/٢٠١٧/٢٠١٨/٢٠١٩

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

This vaccine should be administered in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Paediatric population

- Primary vaccination:

Primary vaccination is achieved with one vaccine dose of 0.5 mL.

- Booster:

A 0.5 ml booster dose is recommended to ensure long-term protection. This booster dose should be administered 6 months to 10 years after the primary vaccination (see section 5.1).

In a context of high to intermediate endemicity, a single-dose or two-dose regimen (primary vaccination and booster) may be used in childhood vaccination programmes in accordance with the WHO recommendations.

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 thrombocytopenia 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 Contraindications

- 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.

6.2 Special warnings and precautions 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.

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

AVAXIM 80 U PEDIATRIC, suspension for injection in prefilled syringe contains phenylalanine, ethanol, potassium and sodium

AVAXIM 80 U PEDIATRIC contains 10 micrograms of phenylalanine in each 0.5 mL dose, which is equivalent to 0.17 micrograms/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.

AVAXIM 80 U PEDIATRIC contains 2 mg of alcohol (ethanol) per dose of 0.5 mL. The quantity for 1 dose of this medicinal product is equivalent to less than 0.1 mL of beer or less than 0.1 mL of wine. The small quantity of alcohol contained in this medicinal product is not likely to cause any notable effects.

AVAXIM 80 U PEDIATRIC contains less than 1 mmol (39 mg) of potassium and less than 1 mmol (23 mg) of sodium per dose, that is to say essentially "potassium-free" and "sodium-free".

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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 Fertility, 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.

Breast-feeding

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

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

a. Summary of the safety profile

More than 6200 children aged from 12 months to 15 years were vaccinated with AVAXIM 80 U PEDIATRIC during clinical trials.

Most undesirable effects were moderate and limited 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.

b. Tabulated list of adverse reactions

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 ($\geq 1/10$)

Common ($\geq 1/100, < 1/10$)

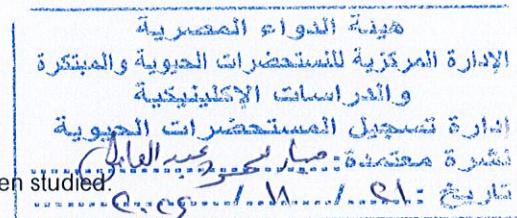
Uncommon ($\geq 1/1\,000, < 1/100$)

Rare ($\geq 1/10\,000, < 1/1000$)

Very rare ($< 1/10\,000$)

Not known: cannot be estimated from the available data.

The table below summarize the frequencies of the adverse reactions that were recorded after the first dose, after the booster dose or after any dose of AVAXIM 80 U PEDIATRIC.



Adverse reactions	Frequency after the primary dose	Frequency after the booster dose	Frequency after any dose
Immune system disorders			
Anaphylactic reaction	Not known	Not known	Not known
Metabolism and nutrition disorders			
Appetite decrease	Common	Common	Common
Psychiatric disorders			
Abnormal crying	Very common	Uncommon	Very common
Irritability	Common	Common	Common
Insomnia	Common	Common	Common
Nervous system disorders			
Cephalalgia	Common	Common	Very common
Vasovagal syncope in response to injection	Not known	Not known	Not known
Seizures with or without fever	Not known	Not known	Not known
Gastrointestinal disorders			
Abdominal pain	Common	Common	Common
Diarrhoea	Common	Common	Common
Nausea	Common	Common	Common
Vomiting	Common	Common	Common
Skin and subcutaneous tissue disorders			
Rash	NR*	Uncommon	Uncommon
Urticaria	Uncommon	NR*	Uncommon
Musculoskeletal and connective tissue disorders			
Arthralgia	Common	Uncommon	Common
Myalgia	Common	Common	Common
General disorders and administration site conditions			
<i>Local reactions</i>			
Pain at the injection site	Very common	Common	Very common
Redness at the injection site	Common	Common	Common
Induration or oedema at the injection site	Common	Common	Common
Haematoma at the injection site	Common	Uncommon	Common
<i>Systemic reactions</i>			
Malaise	Common	Common	Very common
Fever	Common	Common	Common
Asthenia or somnolence	Common	Common	Common

* Not reported during clinical studies

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 : "Agence nationale de sécurité du médicament et des produits de santé (ANSM) et réseau des Centres Régionaux de Pharmacovigilance – Site internet : www.signalement-sante.gouv.fr".

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, purified and then inactivated by formaldehyde.

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 نشرة محدثة: صادر根据公佈的
 تاريخ: ٢٠١٨ / ١١ / ٢٠١٨

It confers immunity against hepatitis A virus (HAV) by inducing anti-HAV antibody titres longer lasting and higher than those obtained after passive immunisation with immunoglobulins. This vaccine has been demonstrated to elicit protective anti-HAV antibody titres (≥ 20 mIU/mL) within two weeks following the injection in over 95% of individuals and in 100% of individuals before the booster dose administered 6 months after the first dose.

Two studies were conducted in Argentina (a region with intermediate endemicity for hepatitis A) to assess the long-term persistence of anti-HAV antibodies.

One study (HAF83) was conducted in children (n = 54) aged 12 months to 47 months vaccinated with two doses of Avaxim 80 U Paediatric six months apart. The results show antibody persistence up to 14–15 years of age at levels considered to be protective and do not suggest the need for further vaccine administrations.

A mathematical model using the available data from this study until 14–15 years after administration of the 2 doses of Avaxim 80 U Pediatric predicts a persistence of the protective anti-HAV antibodies for at least 30 years in 87.5% (CI 95%: 74.1; 94.8) of these children.

Another non-interventional study (HAF82) was conducted in children aged 11 to 23 months at the time of enrolment. All the children received routine vaccination with one dose (group 1: n = 436) or two doses (group 2: n = 108) of hepatitis A vaccine. After 10 years of follow-up, all the available subjects in both groups showed seroprotective levels (anti-HAV antibodies concentration ≥ 3 mIU/ml, using the ECLIA method). Statistical modelling based on the results of the HAF82 study including a natural booster effect predicted similar persistence of anti-HAV protective antibody titres up to 30 years, following administration of one or two doses in over 89% (CI 95%: 80; 96) to 85% (CI 95%: 70; 95) of subjects respectively.

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 excipients

2-Phenoxyethanol, ethanol, formaldehyde and Hanks Medium 199*, water for injections, polysorbate 80, hydrochloric acid and sodium hydroxide for pH adjustment.

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

6.2 Incompatibilities

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

6.3 Shelf-life

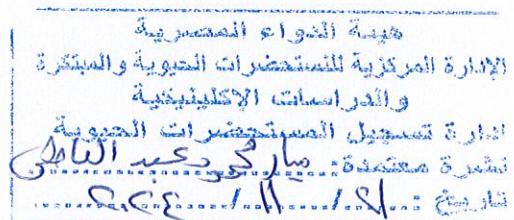
3 years

6.2 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Do not freeze.

Keep in the original packaging, protected from light.



6.5 Nature and contents of container

0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl), with attached needle, without needle or with two separate needles. Box of 1, 10 or 20.

All pack sizes may not be marketed.

6.6 Special precautions for disposal and other 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 medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI PASTEUR

14 ESPACE HENRY VALLÉE
69007 LYON

8. MARKETING AUTHORISATION NUMBER(S)

- 34009 356 772 4 2: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) with one attached needle. Box of 1.
- 34009 356 774 7 1: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) with one attached needle. Box of 10.
- 34009 356 775 3 2: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) with one attached needle. Box of 20.
- 34009 356 777 6 1: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) without needle. Box of 1.
- 34009 356 779 9 0: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) without needle. Box of 10.
- 34009 356 780 7 2: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) without needle. Box of 20.
- 34009 224 595 8 5: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) with two separate needles. Box of 1.
- 34009 224 596 4 6: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) with two separate needles. Box of 10.
- 34009 224 597 0 7: 0.5 mL of suspension in pre-filled syringe (type I glass), with a plunger-stopper (chlorobutyl or bromobutyl) with two separate needles. Box of 20.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[to be completed later by the holder]

10. DATE OF REVISION OF THE TEXT

June 2023

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

الدواء الم dexadrine
الادارة المركزية للمستحضرات المخربة والمعتمدة
والدراسات الاكلينيكية
ادارة تسجيل المستحضرات المخربة
شهر مارس ٢٠٢٣: ميلاد كوكب العامل
الرقم: ١٢٣٤٥٦٧٨٩٠