HEPATITIS A VACCINE (HUMAN DIPLOID CELL), INACTIVATED
[INSTRUCTION]

Name of the Medicinal Product

Healive®, suspension for injection in a pre-filled syringe or in a vial.

Hepatitis A Vaccine (Human Diploid Cell), Inactivated

Quality and Quantitative Composition

Each 1.0 mL dose for adult use contains:

Inactivated HAV antigen (TZ84 strain) [1, 2].....500u[3]

Each 0.5 mL dose for pediatric use contains:

Inactivated HAV antigen (TZ84 strain) [1, 2].....250u[3]

[1] produced in human diploid (2BS) cells

[2] adsorbed on aluminum hydroxide

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

Excipients: aluminum (as aluminum hydroxide), sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium chloride and water for injection.

No preservative is used in Healive®.

Pharmaceutical Form

Suspension for injection in a pre-filled syringe or in a vial.

Hepatitis A Vaccine (Human Diploid Cell), Inactivated is a slightly milky-white suspension.

Therapeutic Indication

Healive® 1.0 mL dose is indicated for active immunization against infection caused by hepatitis A virus in susceptible adults and adolescents of 16 years of age and above, and 0.5 mL dose in children over 1 but below 16 years old.

The use of Healive® should be based on official recommendations.

Posology and Method of Administration

Posology

Recommended dosage and schedule are presented as below:

Age Group	Dosage	Number of Doses	Injection Route
≥ 16 years old	500 u / 1.0 mL	2 (6 months interval)	i.m
>1 but < 16 years old	250 u / 0.5 mL	2 (6 months interval)	i.m

In order to provide long-term protection, a second dose (booster) of a Hepatitis A Vaccine (Human Diploid Cell), Inactivated should be given. The second dose is preferably given 6-12 months after the first dose.

Method of Administration

Healive® should be administered by intramuscular injection in the deltoid region.

Contraindications

- Subjects with known allergic reaction to any component of the vaccine, including excipients, formaldehyde and gentamycin sulfate.

Special Warning and Precautions for Use

- Vaccination shall be postponed to subjects with acute diseases, severe chronic diseases, and chronic diseases at acute attack stage or fever.
- Healive® should be given with caution to individuals on anticoagulant therapy.
- Do not use the vaccine if the container shows abnormalities, such as crack, illegible label, exceeding expiry date or turbidity.
- The vaccine shall be administered immediately after the container is opened.
- Appropriate medical treatments, such as Adrenaline, should be readily available for immediate use in case of rare severe anaphylactic reaction following vaccination. The recipients shall be observed for at least 30 minutes on site after injection.
- It is possible that subjects may be in the incubation period of a hepatitis A infection at the time of immunisation. It is not known whether Healive® will prevent hepatitis A in such cases.
- Shake well before use.

Interaction with Other Medicinal Products and Other Forms of Interactions

No studies of Healive® on interaction with other medicinal products have been conducted. It is not known whether Healive® can use interaction with other medicinal products.

Pregnancy and Lactation

Pregnancy

Animal reproduction studies have not been conducted with Healive®. It is not known whether Healive® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. However, as with all inactivated viral vaccine, the risks to the foetus are considered to be negligible. Healive® should be given to a pregnant woman only if clearly needed after consult a doctor.

Lactation

It is not known whether Healive® is excreted in human milk. Because many drugs excreted in human milk, caution should be exercised when Healive® is administered to woman at breast feeding.

Effects on Ability to Drive and Use Machine

There is no clinical or scientific data for effects on ability to drive and use machine.

Undesirable Effects

Frequencies per dose are defined as follows:

Very common:	$\geq 10\%$
Common:	$\geq 1\%$ and $< 10\%$
Uncommon:	$\geq 0.1\%$ and $< 1\%$
Rare:	$\geq 0.01\%$ and $< 0.1\%$
Very rare:	$< 0.01\%$

Clinical trial data

Application site disorders

Uncommon: Injection site reaction, such as redness and swelling, Pain at the injection site

Body as a whole-general disorders

Common: Fever

Uncommon: Fatigue

Hearing and vestibular disorders

Rare: ear pain

Immune system disorders

Rare: Anaphylaxis

Nervous system disorders

Uncommon: Headache

Gastrointestinal disorders

Uncommon: Vomiting, Nausea, Abdominal pain

Rare: Diarrhea

Respiratory system disorders

Uncommon: Coughing

Skin and appendages disorders

Rare: Rash

General disorders

Uncommon: Sore throat

Rare: Crying

Post-marketing surveillance

Application site disorders

Induration at the injection site

Psychiatric disorders

Agitation

Nervous system disorders

Convulsions, Tetany, somnolence

Respiratory system disorders

Upper respiratory tract infection

Skin and appendages disorders

Pruritus, Urticaria, Urticaria Acute, Erythema induratum, Anigoedema

Vascular (extracardiac) disorders

Purpura allergic

Overdose

Few cases of overdose have been reported with Healive® during the post-marketing surveillance. Adverse reactions reported following overdose were similar to those reported with normal vaccination.

Pharmacodynamic Properties

Pharmacotherapeutic group: Viral vaccine, ATC code: J07BC02.

Healive® confers immunity against hepatitis A virus by inducing antibody titres greater than those obtained after passive immunization with immunoglobulin. Antibody appears shortly after the first injection and 14 days after vaccination 56.7%-93% of immunocompetent subjects are seroprotected (titre above 20 mIU/mL). One month after the first dose, 69.4%-95.5% of subjects have antibody titres above 20 mIU/mL.

The efficacy of Healive® was evaluated in different community outbreaks. These studies indicated that administration of a single dose of Healive® contributed to termination of the outbreaks. In one study, the peak of HAV outbreak began to decrease in 2 weeks after the primary injection. In another study, the protective efficacy was 100% in students who received vaccination.

In order to ensure long term protection, a booster dose should be given between 6 and 12 months after the primary dose. In clinical trials, virtually all vaccinees were seropositive one month after the booster dose.

The long-term persistence of protective antibody levels to hepatitis A virus after a second dose (booster) of Healive® has not been fully evaluated. Nevertheless, serological data show continuing protection against hepatitis A for up to 5 years in subjects who administrated after the full immunization.

Pharmacokinetic Properties

Not applicable to vaccine for prophylaxis.

Preclinical Safety Data

Long-term toxicity study has been conducted for Healive® on mice and rats. No toxicity was observed in mentioned studies.

Incompatibilities

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

Shelf Life

42 months.

Special Precautions for Storage

Store and transport between +2°C and +8°C, and protect from light. Do not freeze.

Nature and Contents of Container

1.0 mL or 0.5 mL suspension in a pre-filled syringe or vial.

Marketing Authorization Numbers

1.0 mL dose for adult use: GuoYaoZhunZi S20020035

0.5 mL dose for pediatric use: GuoYaoZhunZi S20020069

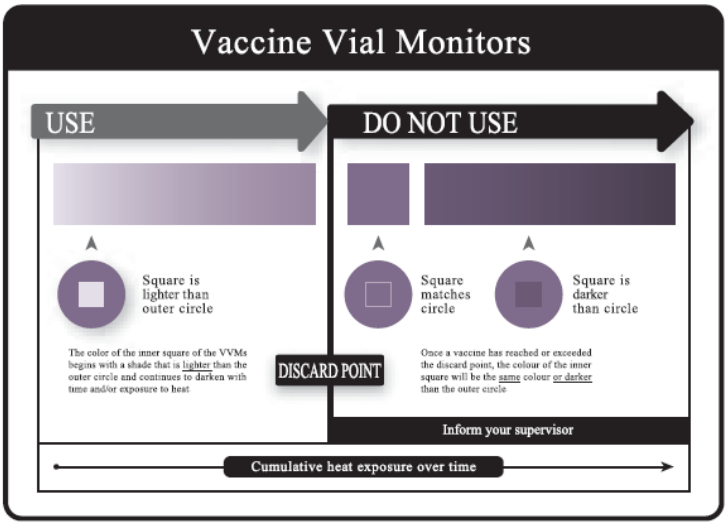
The vaccine satisfies the recommendations given by the World Health Organization in WHO TRS No. 858, Annex 2, 1995 and Pharmacopoeia of the People's Republic of China (Edition 2010).

Vaccine Vial Monitor (see VVM pictogram at the end of the leaflet)

The Vaccine Vial Monitor (VVM) is part of the label used for all Healive® batches supplied by Sinovac. The colour dot that appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

It is absolutely critical to ensure that the storage conditions specified above (in particular the cold chain) are complied with. Sinovac will assume no liability in the event Healive® has not been stored in compliance with the storage instructions. Furthermore Sinovac assumes no responsibility in case a VVM is defective for any reason.



For further information, please contact the manufacturer.

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