Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Healive, Hepatitis A Vaccine (Human Diploid Cell), Inactivated

2. Qualitative and quantitative composition

Each 0.5 ml dose for pediatric use contains:
Inactivated HAV antigen (TZ84 strain) [1], [2].....250 u[3]
[1]produced in human diploid (2BS) cells
[2]adsorbed on aluminium hydroxide
[3]In the absence of an international standardised reference, the antigen content is expressed using an in-house reference.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

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

4. Clinical particulars

4.1 Therapeutic indications

Healive 0.5 ml dose is indicated for active immunization against infection caused by hepatitis A virus, in susceptible children over 1 but below 16 years old. The use of Healive should be based on official recommendations.

4.2 Posology and method of administration

Recommended dosage and schedule are presented as below:

Age Group	Dosage	Number of Doses	Injection Route
>1 but < 16 years old	0.5 ml	2 (6 months interval)	I.M (Deltoid region)

This vaccine confers protection against hepatitis A within two to four weeks. This provides anti-HAV antibodies for at least one year.

Booster vaccination delayed up to 3 years after the primary dose induces similar antibody levels as a booster dose administered within the recommended time interval.

Healive can be used as a booster in subjects previously immunised with any inactivated hepatitis A vaccine.

In the event of a subject being exposed to a high risk of contracting hepatitis

A within two weeks of the primary immunisation dose, human normal immunoglobulin may be given simultaneously with this vaccine at different injection sites.

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.

Current recommendations do not support the need for further booster vaccination among immunocompetent subjects after a 2-dose vaccination course.

4.3 Contraindications

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

4.4 Special warnings 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.

This vaccine shall be administered with caution to the subjects with family or individual history of convulsion and to those with chronic diseases, history of epilepsy, allergic diathesis, as well as to those with severe anaphylactic reaction following a previous injection of this vaccine.

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 immunization. It is not known whether Healive will prevent hepatitis A in such cases.

The vaccine should never be administered intravascularly.

The vaccine should not be administered subcutaneously/intradermally since administration by these routes may result in a less-than-optimal anti-HAV antibody response. In subjects with a bleeding disorder who are

at risk of haemorrhage following intramuscular injection (e.g. haemophiliacs), this vaccine may be administered by deep subcutaneous injection as per local guidance. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

Shake well before use.

4.5 Interaction with other medicinal products and other forms of interaction

Preliminary results suggest that the concomitant administration of a wide variety of other vaccines is unlikely to interfere with the immune response to Healive. This vaccine can be administered simultaneously with vaccines against diphtheria, tetanus, pertussis (DTP), polio (oral and inactivated), Haemophilus influenzae type b (Hib), measles, mumps, rubella, typhoid (oral and intramuscular), hepatitis B, cholera, Japanese encephalitis, rabies and yellow fever, without biologically significant interference in the immunogenicity, reactogenicity or safety of the individual vaccines.

When concurrent administration of other vaccines is required, they should be administered at different sites with different syringes and needles.

No interaction with other medicinal products is currently known.

4.6 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 are excreted in human milk, caution should be exercised when Healive is administered to woman at breast feeding.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The safety profile presented below is based on data from clinical trials, plus reactions observed through post-marketing surveillance. Moreover, the frequency of reactions from the post-marketing data was not possible to calculate.

The most frequently reported reaction is fever, while the next most frequently reported one is pain at site of injection.

Frequencies per dose are defined as follows:

Very common: ≥ 10%

Common: ≥ 1% and < 10%

Uncommon: ≥ 0.1% and < 1%

Rare: ≥ 0.01% and < 0.1%

Very rare: < 0.01%

Not Known: Cannot be estimated from the available data

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Classes	**Frequency**	**Adverse Reaction**
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

System Organ Classes	Frequency	Adverse Reaction
Skin and appendages disorders	Rare	Rash
General disorders	Uncommon	Sore throat

All the above data were calculated based on company-sponsored studies.

Post-marketing surveillance

These adverse reactions were identified through post-marketing surveillance but were not observed in randomized controlled clinical trials.

System Organ Classes	Adverse Reaction
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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 to the local authority.

4.9 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.

5. Pharmacological properties

5.1 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.

5.2 Pharmacokinetic properties

Not applicable to vaccine for prophylaxis.

5.3 Preclinical safety data

Not applicable to vaccine products.

6. Pharmaceutical Particulars

6.1 List of Excipients

Aluminum (as aluminum hydroxide) – 0.625 mg/dosage unit
Disodium hydrogen phosphate – q.s.
Sodium chloride – 4.5 mg/ dosage unit
Sodium dihydrogen phosphate – q.s.
Water for injection – 0.5 ml/ dosage unit

6.2 Incompatibilities

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

6.3 Shelf-Life

36 months.

6.4 Special Precautions for storage

Store and ship at 2-8℃,
Store in the original package to protect it from light.
Do not freeze.

6.5 Nature and Content of container

0.5 ml suspension in a pre-filled syringe (neutral glass Type I) with plunger-stopper (chlorobutyl), staked needle and needle shield (polystyrol) in pack size of 1.

Packs of 200 syringes to a carton.

0.5 ml suspension in a vial (neutral borosilicate glass) with stopper (halogenated butyl rubber) and cap (aluminium-plastics) in pack size of 1.
Packs of 400 vials to a carton.

Not all pack sizes and presentations may be marketed.

6.6 Special precautions for disposal and other handling

Handling instructions
The vaccine should be inspected visually for particulate matter and discolouration prior to administration. Discard the vial if the solution is discoloured or visible particles are observed.
The vial and the pre-filled syringe should be inspected visually for cracks or any abnormalities, such as evidence of tampering prior to administration. In the event of visual cracks or abnormalities, do not administer the vaccine.

Where a full 0.5 ml dose cannot be extracted, the remaining volume should be discarded. Do not pool excess vaccine from multiple vials.
This vaccine does not contain any preservative; it shall be administered immediately after opening.

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

7. Marketing Authorization Holder

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No.15, Zhi Tong Road, Changping Science Park, Changping District, Beijing-102200, P.R.China

8. Marketing Authorization Number

CTD11681

9. Date of first authorization/renewal of the authorization

Date of Renewal, May 26, 2015

10. Date of revision of the text

16/05/2025