



Summary of Product Characteristics

Doc. Name : Summary of Product Characteristics

Department: : Quality Assurance Department (QAD)



Table of Contents

1.	Name of the Medicinal Product	3
2.	Quality and Quantitative Composition	3
3.	Pharmaceutical Form	3
4.	Clinical Particulars	3
4.1	Therapeutic Indication	3
4.2	Posology and Method of Administration	3
4.3	Contraindication	4
4.4	Special Warning and Precautions for Use	4
4.5	Interaction with Other Medicinal Products and Other Forms of Interactions	4
4.6	Pregnancy and Lactation	4
4.7	Effects on Ability to Drive and Use Machine	5
4.8	Undesirable Effects	5
4.9	Overdose	6
5.	Pharmacological Properties	6
5.1	Pharmacodynamic Properties	6
5.2	Pharmacokinetic Properties	7
5.3	Preclinical Safety Data	7
6.	Pharmaceutical Particulars	7
6.1	List of Excipients	7
6.2	Incompatibilities	7
6.3	Shelf Life	7
6.4	Special Precautions for Storage	8
6.5	Nature and Contents of Container	8
7.	Marketing Authorization Holder	8
8.	Marketing Authorization Numbers	8
9.	Date of Authorization	8
10.	Date of Revision of the Text	8



1. 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

2. Quality and Quantitative Composition

Each 1.0 ml dose for adult use contains:

Inactivated HAV antigen (TZ84 strain)^{1,2} 500 u³

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

Excipient(s):

For a full list of excipients, see section 6.1.

3. 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.

4. Clinical Particulars

4.1 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.

The use of Healive should be based on official recommendations.

4.2 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	1.0 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.



4.3 Contraindication

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

4.4 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.

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.

Shake well before use.

4.5 Interaction with Other Medicinal Products and Other Forms of Interactions

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. (WHO position paper, June 2012)

When concurrent administration of other vaccines or IG 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

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 Machine

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: $\geq 10\%$

Common: $\geq 1\%$ and $< 10\%$

Uncommon: $\geq 0.1\%$ and $< 1\%$

Rare: $\geq 0.01\%$ 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
	Rare	Crying

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

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

6. Pharmaceutical Particulars

6.1 List of Excipients

Aluminum (as aluminum hydroxide) – 1.25 mg/dosage unit

Disodium hydrogen phosphate – q.s.

Sodium chloride – 9 mg/ dosage unit

Sodium dihydrogen phosphate – q.s.

Water for injection – 1.0 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

42 months.



6.4 Special Precautions for Storage

Store and ship at 2-8°C, protected from light. Do not freeze.

6.5 Nature and Contents of Container

1.0 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.

1.0 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.

7. Marketing Authorization Holder

Sinovac Biotech Co., Ltd.

No.39, Shangdi Xi Road, Haidian District, Beijing-100085, P.R.China

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

8. Marketing Authorization Numbers

Specification	CFDA Drug Approval Number
1.0 ml dose	GuoYaoZhunZi S20020035

9. Date of Authorization

Specification	Date of First Registration in China	Date of Renewal
1.0 ml dose	May 27, 2002	May 26, 2015

10. Date of Revision of the Text

February 1, 2016