SUMMARY OF PRODUCT CHARACTERISTICS

Havisure®

[ATC Code: J07BC02]

December 2023

Manufactured by

HUMAN BIOLOGICALS INSTITUTE
(A Division of Indian Immunologicals Ltd.)
Rakshapuram, Gachibowli post,
Hyderabad-500032, Telangana, India
Web: www.indimmune.com

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Brand Name: Havisure®

Generic Name: Inactivated Hepatitis A Vaccine (Adsorbed) I.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition

Each 1mL contains:

Inactivated Hepatitis A antigen	NLT 25 IU
Aluminium content as Al $(OH)_3$	NMT 1.25 mg
Tween 20	≤ 0.006 % w/v
Phosphate buffer saline	q.s.

(*For list of excipients, see section 6.1*)

3. PHARMACEUTICAL FORM

- Liquid suspension for intramuscular injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- For Prevention of Hepatitis A infection in children above 1 year, adolescents and adults (19 years to 49 years of age).

4.2. Posology and method of administration

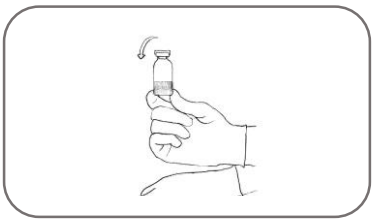
Posology:

- Children above 1 year of age and adolescents: Two doses of 0.5 mL each at an interval of 6 months.
- Adults (19 years to 49 years of age): Two doses of 1 mL each at an interval of 6 months.

Administration:

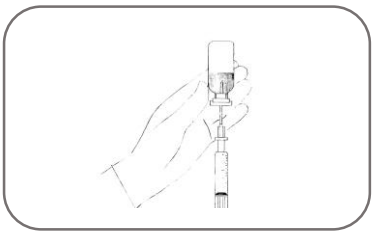
The liquid vaccine vial should be gently shaken before use to homogenize the suspension. The site of administration must be sterilized by alcohol swab which should be allowed to evaporate before injection. The required dose of 0.5 ml or 1.0 ml of the vaccine, as per the age group, should be withdrawn and administered intramuscularly (in deltoid region in adults and older children and in the anterolateral aspect of thigh in the younger children). When using the vaccine for two paediatric doses, after taking one paediatric dose, if second person is not immediately present, the remaining 0.5 ml of the vaccine should be discarded.

1



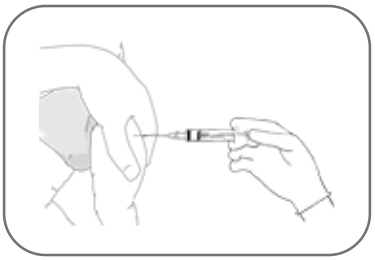
Mixing of the content of the vial before withdrawal into syringe

2



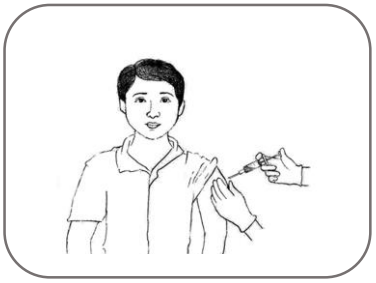
Withdrawal of the vaccine into the syringe before administration

3



Intramuscular Administration in younger children

4



Intramuscular Administration in older children & Adults

4.3. Contraindications

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any Hepatitis A containing vaccine, or to any component of the Inactivated Hepatitis A vaccine (Adsorbed).
- As with other vaccines, the administration of the Inactivated Hepatitis A vaccine (Adsorbed) should be postponed in subjects with severe febrile illness. The presence of a minor infection, however, is not a contraindication.

4.4. Special warnings and precautions for use

Warnings:

- Since Hepatitis A virus has a long incubation period, the Inactivated Hepatitis A vaccine (Adsorbed) may not prevent infection, if the vaccinee is already harboring an unrecognized Hepatitis A infection at the time of immunization.
- In immunocompromised persons and individuals receiving immunosuppressant therapy immune response to the Inactivated Hepatitis A vaccine (Adsorbed) may be diminished.
- The Inactivated Hepatitis A vaccine (Adsorbed) should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Precautions:

- The vaccinee should be observed for 30 to 60 minutes after administration of vaccine for any immediate reactions. This would help in prompt management of the adverse reaction, if any, and can be potentially reversed with proper and timely treatment.
- For anaphylactic reactions, adrenaline/ epinephrine (1 in 1000) may be used. For treatment of severe anaphylaxis the initial dose of adrenaline is 0.1-0.5 mg (0.1-0.5 mL of 1:1000 injection) given s/c or i/m. Single adult dose should not exceed 1 mg (1 mL). For children the recommended dose of adrenaline is 0.01 mg/kg (0.01mL/kg of 1:1000 injection). Single paediatric dose should not exceed 0.5 mg (0.5mL).
- Syncope can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury in such scenario.
- Antihistamines, hydrocortisone, IV fluids and other appropriate medications should also be used as per requirement.
- *Care should be taken to ensure that needle does not enter into a blood vessel.*

4.5. Interactions with other medicinal products and other forms of interactions

- If indicated and advised, Inactivated Hepatitis A vaccine (Adsorbed) may be administered concomitantly with immunoglobulin. When concomitant administration of other vaccines or immunoglobulin is required, they should be given with different syringes and at different injection sites. Hepatitis A vaccine (Adsorbed) should not be mixed with any other vaccine or product in the same syringe or vial.
- Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater-than-physiologic doses), may reduce the immune response to Inactivated Hepatitis A vaccine (Adsorbed).

4.6. Fertility, Pregnancy and Lactation

The safety of the vaccine in pregnant and lactating mothers has not been established yet.

4.7. Effects on ability to drive and use machines

There has been no reported case of any effect of administration of Inactivated Hepatitis A vaccine (Adsorbed) on driving or using machines.

4.8. Undesirable effects

The Inactivated Hepatitis A vaccine (Adsorbed) is generally well tolerated.

The following adverse events have been observed in clinical trials involving Inactivated Hepatitis A vaccine (Adsorbed):

Local (at the injection site) reactions: Injection site Pain, Injection site Erythema (Redness) and Injection site Swelling.

Systemic reactions: Fever, Headache, Fatigue (Tiredness), Malaise (Feeling Unwell), Anorexia (Decreased Appetite), Gastroenteritis, Nausea and Diarrhoea.

As with any other vaccine, there is a rare chance of allergic reaction including anaphylaxis.

4.9. Overdose

There has been no report of overdose with the Inactivated Hepatitis A vaccine (Adsorbed).

5. PHARMACOLOGICAL PROPERTIES

Mechanism of Action:

The Inactivated Hepatitis A vaccine (Adsorbed), after administration, induces production of specific antibodies against the Hepatitis A virus. These antibodies result in protection from Hepatitis A infection.

5.1. Pharmacodynamic properties

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Administration of the Inactivated Hepatitis A vaccine (Adsorbed) stimulates the immune system of the body. The immune response thus elicited includes production of protective antibodies against Hepatitis A virus in the body. The immune response is considered seroprotective if the anti-HAV antibody (IgG) titre is ≥ 20 mIU/ ml.

In an open label Phase I study conducted in India, the safety and immunogenicity of the vaccine was evaluated when administered as a single dose in two groups of healthy subjects: 33 subjects in the age group of 19 to 49 years (Group A) and 22 subjects in 12 to 18 years of age (Group B). No Serious adverse event (SAE) was reported during the study. Among the local adverse events, Pain at the injection site (20%) was the only adverse event reported. Among the systemic adverse events, Fatigue (9.1%) and Headache (9.1%) were the most common Systemic adverse events reported followed by Diarrhoea (6.1%), Fever (6.1%), Anorexia (3.0%) and Nausea (3.0%). All the adverse events were of mild severity except for 2 events which were of moderate severity. There was 100% seroconversion and seroprotection for all the subjects who

completed the study as per protocol. In Group A, the Geometric mean titre significantly increased from 3.9 mIU/ml (Pre-vaccination) to 560.9 mIU/ml (Post vaccination). Similarly in Group B, the Geometric mean titre significantly increased from 2.03 mIU/ml (Pre-vaccination) to 304.5 mIU/ml (Post vaccination).

In Phase II/III Clinical trial conducted in India, immunogenicity and safety of the vaccine were studied when administered to two age groups of healthy subjects: 176 subjects in the age group of 19- 49 years (Group A) and 176 subjects from 12 months to below 19 years of age (Group B). There was 100% seroprotection and seroconversion in all the subjects who completed the study. In Group A, the Geometric mean titre increased from pre-vaccination level of 3.17 mIU/mL to 428.37 mIU/mL post vaccination and in Group B, the Geometric mean titre increased from pre-vaccination level of 5.46 mIU/mL to 420.86 mIU/mL post vaccination. No Serious adverse event (SAE) was reported during the study. Among the local adverse events, Injection site Pain (14.49%) was the most common adverse event followed by Injection site Swelling (3.69%) and Injection site Erythema (1.14%). Among the systemic adverse events, Fever (Pyrexia) (3.69%) was the most common adverse event followed by Headache (1.70%), Gastroenteritis (0.57%), Malaise (0.28%), Decreased appetite (Anorexia) (0.28%) and Tiredness (0.28%). All the adverse events were of mild severity except for 2 events which were of moderate severity.

5.2. Pharmacokinetic properties

Not applicable.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Aluminium content as $Al(OH)_3$
Tween-20
Phosphate buffer saline

6.2. Incompatibilities

The vaccine should not be mixed with any other product for administration.

6.3. Shelf life

36 months from the date of manufacture.

6.4. Special precautions for storage

- Keep out of reach of Children.
- Store and transport between +2° C and +8° C.
- Shake well before use.
- DO NOT FREEZE. Discard vaccine vial if frozen.
- Do not keep the vaccine along with other medicinal product including other vaccine(s) that could create confusion and lead to admixture.

6.5. Nature and contents of container

- 1.0 ml vial (single adult dose/ two pediatric doses)

6.6. Special precautions for disposal and other handling

(A) Disposal:

Dispose as per the applicable Biomedical Waste Disposal guidelines/ rules.

(B) Other Handling:

- Use new sterile syringe and needle for every administration.
- Alcohol and other disinfecting agents must be allowed to evaporate from skin before injection of vaccine.
- The vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration. In the event of either being observed, the vaccine must be discarded.
- When using the vaccine for two pediatric doses, after taking one pediatric dose, if second person is not immediately present, the remaining 0.5 ml of the vaccine should be discarded.

7. MARKETING AUTHORISATION HOLDER

Human Biologicals Institute
(A Division of Indian Immunologicals Limited)
Rakshapuram, Gachibowli Post,
Hyderabad-500 032, INDIA.
Web : www.indimmune.com

8. MARKETING AUTHORISATION NUMBER

The Marketing Authorization Number is country specific. In India, the country of origin, the Marketing Authorization Number is: 02/RR/AP/2005/V/R.

9. DATE OF FIRST AUTHORISATION

Date of First Authorization in India, the country of origin: September 2023.

10. DATE OF COMPILATION OF THE TEXT

December 2023