

PRODUCT MONOGRAPH

HAVRIX[®]

Hepatitis A vaccine, inactivated

Suspension for injection

Active immunizing agent
against infection by hepatitis A virus

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4

Date of Approval:
July 12, 2011

Submission Control No: 147365

© 2011 GlaxoSmithKline Inc. All Rights Reserved

® HAVRIX and ® ENGERIX-B are registered trademarks, used under license by GlaxoSmithKline Inc.

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION.....	3
SUMMARY PRODUCT INFORMATION	3
DESCRIPTION.....	3
INDICATIONS AND CLINICAL USE.....	3
CONTRAINDICATIONS	5
WARNINGS AND PRECAUTIONS.....	5
ADVERSE REACTIONS.....	6
DOSAGE AND ADMINISTRATION	8
OVERDOSAGE	10
ACTION AND CLINICAL PHARMACOLOGY	10
STORAGE AND STABILITY.....	11
DOSAGE FORMS, COMPOSITION AND PACKAGING	11
PART II: SCIENTIFIC INFORMATION	13
PHARMACEUTICAL INFORMATION.....	13
CLINICAL TRIALS.....	13
DETAILED PHARMACOLOGY	15
MICROBIOLOGY	15
TOXICOLOGY	15
REFERENCES	15
PART III: CONSUMER INFORMATION.....	19

HAVRIX®

Hepatitis A vaccine, inactivated

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intramuscular Injection	Sterile suspension for injection/ HAVRIX® 1440 contains: 1440 ELISA units per 1.0 mL of formaldehyde-inactivated hepatitis A virus (HM175 hepatitis A virus strain); HAVRIX® 720 Junior contains: 720 ELISA units per 0.5 mL of formaldehyde-inactivated hepatitis A virus (HM175 hepatitis A virus strain).	Aluminum hydroxide, amino acids for injection, disodium phosphate, monopotassium phosphate, neomycin sulphate, polysorbate 20, potassium chloride, sodium chloride and water for injection.

DESCRIPTION

HAVRIX® (hepatitis A vaccine, inactivated) is a sterile suspension containing formaldehyde-inactivated hepatitis A virus (HM175 hepatitis A virus strain) adsorbed onto aluminum hydroxide.

INDICATIONS AND CLINICAL USE

HAVRIX® (hepatitis A vaccine, inactivated) is indicated for:

- active immunization against hepatitis A virus (HAV) infection in subjects at risk of exposure to HAV.

HAVRIX[®] will not prevent hepatitis infection caused by other agents such as hepatitis B virus, hepatitis C virus, hepatitis E virus or other pathogens known to infect the liver.

In areas of **low to intermediate prevalence** of hepatitis A, immunization with HAVRIX[®] is particularly recommended in subjects who are, or will be, at increased risk of infection such as:

Travelers: Persons traveling to areas where the prevalence of hepatitis A is high. These areas include Africa, Asia, the Mediterranean basin, the Middle East, Central and South America.

Armed Forces: Armed Forces personnel who travel to higher endemicity areas or to areas where hygiene is poor have an increased risk of HAV infection. Active immunization is indicated for these individuals.

Persons for whom Hepatitis A is an Occupational Hazard: These include employees in day-care centres, nursing, medical and paramedical personnel in hospitals and institutions, especially gastroenterology and pediatric units, sewage workers, and food handlers, among others.

Persons for whom there is an Increased Risk of Transmission of Hepatitis A: e.g. homosexuals, persons with multiple sexual partners, abusers of injectable drugs, hemophiliac patients.

Contacts of Infected Persons: Since virus shedding of infected persons may occur for a prolonged period, active immunization of close contacts is recommended.

Specific Population Groups known to have Higher Incidence of Hepatitis A: e.g. North American Indians, Inuits, recognized community-wide HAV epidemics.

Subjects with chronic liver disease or who are at risk of developing chronic liver disease e.g. Hepatitis B (HB) and Hepatitis C (HC) chronic carriers and alcohol abusers. Hepatitis A tends to compromise the outcome of chronic liver disease.

In areas of **intermediate to high prevalence** of hepatitis A (e.g. Africa, Asia, the Mediterranean basin, the Middle East, Central and South America) susceptible individuals may be considered for active immunization.

CONTRAINDICATIONS

HAVRIX[®] (hepatitis A vaccine, inactivated) should not be administered:

- to subjects with known hypersensitivity to any component of the vaccine preparation or component of the container, or to subjects having shown signs of hypersensitivity after previous HAVRIX[®] administration. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the product monograph.

As with other vaccines, the administration of HAVRIX[®] should be postponed in subjects with severe febrile illness. The presence of a minor infection however, is not a contraindication.

WARNINGS AND PRECAUTIONS

General

As with other injectable vaccines, appropriate medication (e.g. adrenaline) should be readily available for immediate use in case of anaphylaxis or anaphylactoid reactions following administration of the vaccine. For this reason, the vaccinee should remain under medical supervision for 30 minutes after immunization.

Syncope (fainting) 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 from faints.

Hematologic

HAVRIX[®] (hepatitis A vaccine, inactivated) should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Immune

It is possible that subjects may be in the incubation period of hepatitis A infection at the time of immunization. It is not known whether HAVRIX[®] will prevent hepatitis A in such cases.

Since there is a possibility that the vaccine may contain trace amounts of neomycin, the possibility of an allergic reaction in individuals sensitive to this substance should be kept in mind when considering the use of this vaccine (see DOSAGE FORMS, COMPOSITION AND PACKAGING).

As with other vaccines, subjects with an impaired immune system may not obtain adequate antibody titres after the primary immunization course. Such patients may require administration of additional doses of HAVRIX[®]. However, no specific dosing recommendations can be made at this time.

Renal

As with other vaccines, hemodialysis patients may not obtain adequate antibody titres after the primary immunization course. Such patients may require administration of additional doses of HAVRIX[®]. However, no specific dosing recommendations can be made at this time.

Special Populations**Pregnant Women:**

Animal reproduction studies and adequate human data on use during pregnancy are not available. However, as with all inactivated viral vaccines, the risks to the fetus are considered to be negligible. HAVRIX[®] should be used during pregnancy only when clearly needed.

Nursing Women:

Animal reproduction studies and adequate human data on use during lactation are not available. Therefore, caution should be exercised if HAVRIX[®] is to be administered to breast feeding women.

ADVERSE REACTIONS**Clinical Trial Adverse Drug Reactions**

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The safety profile presented below is based on data from more than 5300 subjects.

Frequency of doses	Adverse Event	System/Organ Class
Very Common: ≥ 10%	Irritability	Psychiatric disorders
	Headache	Nervous system disorders
	Pain and redness at the injection site, fatigue	General disorders and administration site conditions
Common: ≥ 1% and < 10%	Appetite loss	Metabolism and nutrition disorders
	Drowsiness	Nervous system disorders
	Gastrointestinal symptoms (such as nausea, vomiting, diarrhea)	Gastrointestinal disorders
	Swelling at the injection site, malaise, injection site reaction (such as induration), fever (≥ 37.5°C)	General disorders and administration site conditions
Uncommon: ≥ 0.1% and < 1%	Upper respiratory tract infection, rhinitis	Infections and infestations
	Dizziness	Nervous system disorders
	Rash	Skin and subcutaneous tissue disorders
	Myalgia, musculoskeletal stiffness	Musculoskeletal and connective tissue disorders
	Influenza-like illness	General disorders and administration site conditions
Rare: ≥ 0.01% and < 0.1%	Hypoaesthesia, paraesthesia	Nervous system disorders
	Pruritus	Skin and subcutaneous tissue disorders
	Chills	General disorders and administration site conditions

Post-Market Adverse Drug Reactions

The following adverse reactions have been reported with HAVRIX[®].

Immune system disorders	Anaphylaxis, allergic reactions including anaphylactoid reactions and mimicking serum sickness
Nervous system disorders	Convulsions
Vascular disorders	Vasculitis
Skin and subcutaneous tissue disorders	Angioneurotic oedema, urticaria, erythema multiforme
Musculoskeletal and connective tissue disorders	Arthralgia

DRUG INTERACTIONS

Overview

Since HAVRIX[®] is an inactivated vaccine, its concomitant use with other inactivated vaccines is unlikely to result in interference with immune responses. When concomitant administration of other vaccines is considered necessary, the vaccines must be given with different syringes and at different injection sites.

Clinical experiences with the concomitant administration of HAVRIX[®] and the recombinant hepatitis B virus vaccine, ENGERIX[®]-B, has been satisfactory. No interference in the respective immune responses to both antigens has been observed.

Concomitant administration of typhoid, yellow fever, cholera (injectable) or tetanus does not interfere with HAVRIX[®] immune response.

HAVRIX[®] must not be mixed with other vaccines.

Drug-Drug Interactions

The concomitant administration of HAVRIX[®] (hepatitis A vaccine, inactivated) and immune globulin (human) does not influence the seroconversion rate, but may result in a relatively lower anti-HAV antibody titre than when the vaccine is given alone.

HAVRIX[®] and immune globulin (human) should be administered at separate injection sites.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

Primary Immunization

Adults from 19 years onwards

A single dose of HAVRIX[®] 1440 (hepatitis A vaccine, inactivated) (1.0 mL suspension) is used for primary immunization.

Children and adolescents from 1 year up to and including 18 years of age

A single dose of HAVRIX[®] 720 Junior (0.5 mL suspension) is used for primary immunization. If a pediatric vial is not available, a pediatric dose of 0.5 mL may be withdrawn from the HAVRIX[®] 1440 vial.

Booster Dose

A booster dose is recommended at any time between 6 and 12 months after a single dose of HAVRIX[®] 1440 or HAVRIX[®] 720 Junior in order to ensure long-term protection.

Long-term persistence of serum antibodies to hepatitis A virus after vaccination with HAVRIX[®] is under evaluation. Nevertheless, data available after 5 years show persistence of antibodies which is consistent with a projected 20 years persistence (based on mathematical calculations).

Concomitant administration with immune globulin (human)

Concomitant administration of HAVRIX[®] and immune globulin (human) may be considered when a subject is at risk of being exposed to hepatitis A before adequate anti-HAV antibody titres can be reached.

Administration

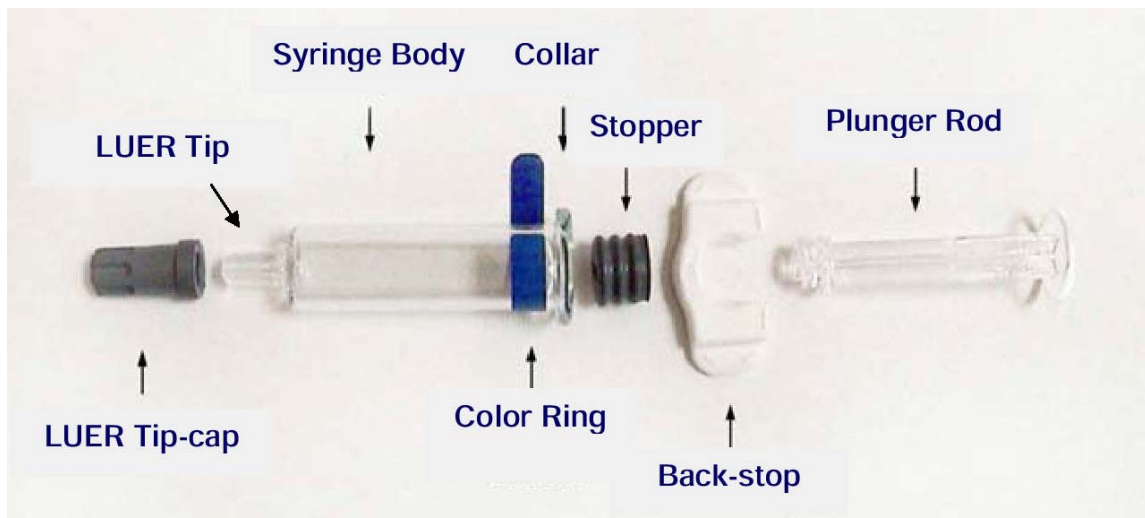
HAVRIX[®] should be injected **intramuscularly** in the deltoid region in adults and children, in the antero-lateral part of the thigh in young children up to 2 years of age. The vaccine **should not** be administered intramuscularly in the gluteal region or subcutaneously/intradermally since administration by these routes may result in a less than optimal anti-HAV antibody response.

As with all parenterals, vaccine products should be inspected visually for any foreign particulate matter and/or discolouration prior to administration. Before use of HAVRIX[®], the vial/syringe should be well shaken to obtain a slightly opaque, white suspension. Discard the vaccine if the contents of the vial/syringe appear otherwise.

The vaccine must be used as supplied.

Syringe Instructions

Do not remove the white back-stop from the syringe. Prior to administration, ensure that the plunger rod is firmly attached to the rubber stopper by turning the plunger clockwise until slight resistance is felt. **Do not** over tighten. Remove syringe LUER Tip-cap and needle cap. Attach needle by pressing and twisting in a clockwise rotation until secured to the syringe.



HAVRIX[®] should never be administered intravenously.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Cases of overdose have been reported during post-marketing surveillance. Adverse events reported following overdosage were similar to those reported with normal vaccine administration.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

HAVRIX[®] (hepatitis A vaccine, inactivated) confers immunity against hepatitis A virus (HAV) infection by inducing the production of specific anti-HAV antibodies.

In clinical studies involving subjects of 18 – 50 years of age, specific humoral antibodies against HAV were detected in more than 88% of vaccinees at day 15 and 99% at month 1 following administration of a single dose of HAVRIX[®] 1440 (hepatitis A vaccine, inactivated).

In clinical studies involving subjects of 1 – 18 years of age, specific humoral antibodies against HAV were detected in more than 93% of vaccinees at day 15 and 99% of vaccinees one month following administration of HAVRIX[®] 720 Junior.

Results of hepatitis A outbreak control program showed a substantial drop in symptomatic cases in 4,930 vaccinees within 3 weeks of receiving 1 dose of hepatitis A vaccine. In villages where more than 70% of estimated susceptible individuals were vaccinated, a dramatic drop in the number of symptomatic cases of disease was observed within 8 weeks of vaccination.

The mean titre of anti-HAV antibodies induced by HAVRIX[®] is at least 3 times higher than the maximum observed after passive immunization using immune globulin (human). In a randomly selected subset of subjects, vaccine induced anti-HAV antibodies were shown to be qualitatively indistinguishable from immune globulin (human) anti-HAV antibodies.

To obtain long-term immunity a booster dose is recommended at any time between 6 and 12 months after primary vaccination with HAVRIX[®] 1440 Adult or HAVRIX[®] 720 Junior, to induce long-term antibody titres.

Long-term persistence of serum antibodies to hepatitis A virus after vaccination with HAVRIX[®] is under evaluation. Nevertheless, data available after 5 years show persistence of antibodies which is consistent with a projected 20 years persistence (based on mathematical calculations).

Primates exposed to the virulent heterologous hepatitis A strain were vaccinated 2 days after exposure. This post exposure vaccination resulted in total protection of the animals.

STORAGE AND STABILITY

The vaccine should not be used beyond the expiry date stamped on the vial or syringe.

HAVRIX[®] (hepatitis A vaccine, inactivated) must be stored at 2 to 8°C.

Do not freeze; discard if vaccine has been frozen.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

HAVRIX[®] (hepatitis A vaccine, inactivated) is available as HAVRIX[®] 1440 (1440 ELISA Units/mL) and HAVRIX[®] 720 Junior (720 ELISA Units/0.5 mL) suspension for injection.

Composition

HAVRIX[®] is a sterile suspension containing formaldehyde-inactivated hepatitis A virus (HM175 hepatitis A virus strain) adsorbed onto aluminum hydroxide.

The virus is propagated in MRC₅ human diploid cells. Before viral extraction, the cells are extensively washed to remove culture medium constituents. A virus suspension is then obtained by lysis of the cells followed by purification using ultrafiltration techniques and gel chromatography. Inactivation of the virus is assured by treatment with formalin. The viral antigen content of HAVRIX[®] is determined by an ELISA test. Each dose is standardized to ensure a viral antigen content of not less than:

	ELISA Units	Dose Volume
HAVRIX [®] 1440	1440	1.0 mL
HAVRIX [®] 720 Junior	720	0.5 mL

The virus is adsorbed on aluminum (0.5 mg/1.0 mL adult dose, 0.25 mg/0.5 mL pediatric dose) in the form of aluminum hydroxide. Other excipients are: aluminum hydroxide, amino acids for injection, disodium phosphate, monopotassium phosphate, neomycin sulphate (less than 10 ng for HAVRIX[®] 720 Junior; less than 20 ng for HAVRIX[®] 1440), polysorbate 20, potassium chloride, sodium chloride, water for injection.

HAVRIX[®] meets the World Health Organization requirement for biological substances including those for final vaccine residual bovine serum albumin.

Packaging

HAVRIX[®] 1440:

Single Dose 1 mL Vials: In packages of 1, 10 or 25 vials.

Single Dose 1 mL Prefilled Syringes: In packages of 1 prefilled syringe.

HAVRIX[®] 720 Junior:

Single Dose 0.5 mL Vials: In packages of 1 or 10 vials.

Single Dose 0.5 mL Prefilled Syringes: In packages of 1 prefilled syringe.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: hepatitis A vaccine, inactivated

Product Characteristics

HAVRIX[®] (hepatitis A vaccine, inactivated) is a sterile suspension containing formaldehyde-inactivated hepatitis A virus (HM175 hepatitis A virus strain) adsorbed onto aluminum hydroxide.

CLINICAL TRIALS

Clinical studies have been conducted in Asia, Europe, Latin America, USA and Canada to evaluate the immunogenicity and reactogenicity of HAVRIX[®].

Summary of Study Demographics, Trial Design and Efficacy Results

Study No.	Trial design	Dosage and route of administration	No. of subjects	Patient Demographics	Immunogenicity Results ¹	
					SC Rate (%)	GMT (mIU/ml)
HAV-104	Double-blind, randomized, multi-country, multi-centre	Intramuscular injection (into deltoid region) 1440 EL.U/1 mL dose 0, 6 month dosing schedule	Enrolled: 150	Healthy adults aged 18 to 50 years	97.6 ²	577 ²
HAV-107	Double-blind, randomized, multi-country, multi-centre	Intramuscular injection (into deltoid region) 1440 EL.U/1 mL dose 0, 6 month dosing schedule	Enrolled: 150	Healthy adults aged 18 to 40 years	99.3 ²	490 ²
HAV-112	Double-blind, randomized, multi-country, multi-centre	Intramuscular injection (into deltoid region) 1440 EL.U/1 mL dose 0, 12 month dosing schedule	Enrolled: 194	Healthy adults aged 21 to 40 years	99.4 ³	387 ³

Study No.	Trial design	Dosage and route of administration	No. of subjects	Patient Demographics	Immunogenicity Results ¹	
					SC Rate (%)	GMT (mIU/ml)
HAV-115	Open randomized, multi-country, multi-centre	Intramuscular injection (into deltoid region) Group 1: 720 EL.U/0.5 mL dose Group 2: 1440 EL.U/1 mL dose 0, 6 month dosing schedule	Enrolled : 202	Healthy adolescents aged 12 to 19 years	Group 1: 99.0 Group 2: 100	Group 1: 249 Group 2: 349
HAV-117B	Open study, multi-country, multi-centre	Intramuscular injection (into deltoid region) 720 EL.U/0.5 mL dose 0, 6 month dosing schedule	Enrolled : 60	Healthy children aged 2 to 13 years	100	305
HAV-118	Open prospective study, multi-country, multi-centre	Intramuscular injection (into deltoid region, and sometimes the thigh muscle) 720 EL.U/0.5 mL dose 0, 12 month dosing schedule	Enrolled : 54	Healthy children aged 2 to 11 years	95.5	184
HAV-122	Open randomized study, multi-country, multi-centre	Intramuscular injection (into deltoid region) 720 EL.U/0.5 mL dose 0, 6 month dosing schedule	Enrolled : 81	Healthy children aged 2 to 15 years	96.8	194
HAV-129	Open study, multi-country, multi-centre	Intramuscular injection (into deltoid region) 720 EL.U/0.5 mL dose 0, 6 month dosing schedule	Enrolled : 120	Healthy adolescents aged 9 to 18 years	100	256
Alaskan Outbreak Control Programme	Independent study, multi-country, multi-centre	Children/teenagers received dose level of 720 EL.U/0.5 mL Adults received dose level of 1440 EL.U/1 mL	Enrolled : 4,930	Mean age (\pm standard deviation): 16.47 \pm 14.9 years Male: 51% Female: 49%	92 ⁴	Children / teenagers: 269 ⁵ Adults: 254 ⁶

1. Results at 1 month after initial dose
2. Average of 3 lots
3. Average of 2 lots
4. Results at 3-4 weeks after initial dose
5. Average for 3 different age groups (1-2 years, 3-9 years and 10-19 years)
6. 20-40 years age group

Efficacy

Clinical studies performed in Europe (HAV 104, 107, 112) evaluated immune response in adults to primary vaccination with HAVRIX[®] 1440. Antibodies were measured at screening, day 15, and at month 1 and 6.

In an overall analysis of immunogenicity following vaccination the seroconversion rate was 98.9% at month 1 and the Geometric Mean Titre was 466 mIU/mL.

Clinical studies performed in Asia, Europe, Latin America, and Alaska (HAV 115, 117B, 118, 122, 129 and Alaskan outbreak program) evaluated immune response in subjects between 2 and 18 years receiving 720 EL.U.

The overall analysis of immunogenicity following vaccination showed that the seroconversion rate was 99.3% at month 1 and the Geometric Mean Titre was 253 mIU/mL.

Safety

For safety information please refer to the Adverse Reactions Section, Part I.

DETAILED PHARMACOLOGY

Not applicable.

MICROBIOLOGY

Not applicable.

TOXICOLOGY

Not applicable.

REFERENCES

1. Atkins M, Zambon M, Watkins P. Hepatitis A virus infection. Should susceptible homosexual men be offered immunization. *BMJ*. 1993;307(6903):562.
2. Chriske H, Abdo R, Richrath R, Braumann S. Hepatitis-A-Infektionsgefährdung bei Kanalund Klärwerksarbeitern [The Risk of Hepatitis-A Infection among Sewer Workers]. *Arbeitsmed*. 1990;25(6):285-287.

3. Cossar JH, Reid D, Fallon RJ, Bell EJ, Riding MH, Follett EA et al. A cumulative review of studies on travellers, their experience of illness and the implications of these findings. *J Infect.* 1990;21(1):27-42.
4. Coutinho RA, Albrecht-van Lent P, Lelie N, Nagelkerke N, Kuipers H, Rijdsdijk T. Prevalence and incidence of hepatitis A among male homosexuals. *Br Med J (Clin Res Ed).* 1983;287(6407):1743-1745.
5. D'Hondt E, Purcell RH, Emerson SU, Wong DC, Shapiro M, Govindarajan S. Efficacy of an inactivated hepatitis A vaccine in pre- and postexposure conditions in marmosets. *J Infect Dis.* 1995;171 Suppl 1:S40-S43.
6. Desenclos JC, MacLafferty L. Community wide outbreak of hepatitis A linked to children in day care centres and with increased transmission in young adult men in Florida 1988-9. *J Epidemiol Community Health.* 1993;47(4):269-273.
7. Frölich J, Zeller I. Hepatitis-A-Infektionsrisiko bei den Mitarbeitern einer grossen Kläranlagenbetreibergenossenschaft. *Abeitsmed.* 1993;28(11):503-505.
8. Germanaud J, Causse X, Barthez JP. Prevalence of antibodies to hepatitis A virus in health care workers. *Eur J Clin Microbiol Infect Dis.* 1993;12(7):572-573.
9. Gerritzen A, Schneewis KE, Brackmann HH, Oldenburg J, Hanfland P, Gerlich WH et al. Acute hepatitis A in haemophiliacs. *Lancet.* 1992;340(8829):1231-1232.
10. Hadler SC, Erben JJ, Francis DP, Webster HM, Maynard JE. Risk factors for hepatitis A in day-care centers. *J Infect Dis.* 1982;145(2):255-261.
11. Hanna J. Hepatitis A in a Child Day-care Centre. *Commun Dis Intell.* 1993;17(4):73-75.
12. Harkess J, Gildon B, Istre GR. Outbreaks of hepatitis A among illicit drug users, Oklahoma, 1984-87. *Am J Public Health.* 1989;79(4):463-466.
13. Hepatitis A among drug abusers. *MMWR Morb Mortal Wkly Rep.* 1988;37(19):297-300, 305.
14. Hesla PE. Hepatitis A in Norwegian troops. *Vaccine.* 1992;10 Suppl 1:S80-S81.
15. Hofmann F, Berthold H, Wehrle G. Immunity to hepatitis A in hospital personnel. *Eur J Clin Microbiol Infect Dis.* 1992;11(12):1195.
16. Hoke CH, Jr., Binn LN, Egan JE, DeFraitess RF, MacArthy PO, Innis BL et al. Hepatitis A in the US Army: epidemiology and vaccine development. *Vaccine.* 1992;10 Suppl 1:S75-S79.

17. Holter E, Siebke JC. Hepatitis A in young Norwegian drug addicts and prison inmates. *Infection*. 1988;16(2):91-94.
18. Keeffe EB. Is hepatitis A more severe in patients with chronic hepatitis B and other chronic liver diseases? *Am J Gastroenterol*. 1995;90(2):201-205.
19. Koster D, Hofmann F, Berthold H. Hepatitis A immunity in food-handling occupations. *Eur J Clin Microbiol Infect Dis*. 1990;9(4):304-305.
20. Kruppenbacker J, Bock H, Bienzle U. Immunogenicity, Safety and Interference of SB Biologicals' Inactivated hepatitis A vaccine with other simultaneously administered travel vaccinations: experience of multicenter trial in Germany. Presented, Fourth International Conference on Travel Medicine. 1995.
21. Mannucci PM. Outbreak of hepatitis A among Italian patients with haemophilia. *Lancet*. 1992;339(8796):819.
22. Mannucci PM, Gdovin S, Gringeri A, Colombo M, Mele A, Schinaia N et al. Transmission of hepatitis A to patients with hemophilia by factor VIII concentrates treated with organic solvent and detergent to inactivate viruses. The Italian Collaborative Group. *Ann Intern Med*. 1994;120(1):1-7.
23. McFarlane ES, Embil JA, Manuel FR, Thieboux HJ. Antibodies to hepatitis A antigen in relation to the number of lifetime sexual partners in patients attending an STD clinic. *Br J Vener Dis*. 1981;57(1):58-61.
24. Rothschild C, Pol S, Mattlinger B, Reijasse D, Torchet MF, Gazengel C. Vaccination against Hepatitis A Virus in French Hemophilic Children. *Vox Sanguinis*. 1995;69(1):80-81.
25. Rubertone MV, DeFraités RF, Krauss MR, Brandt CA. An outbreak of hepatitis A during a military field training exercise. *Mil Med*. 1993;158(1):37-41.
26. Sjogren MH, Tanno H, Fay O, Sileoni S, Cohen BD, Burke DS et al. Hepatitis A virus in stool during clinical relapse. *Ann Intern Med*. 1987;106(2):221-226.
27. Steffen R. Risk of hepatitis A in travellers. *Vaccine*. 1992;10 Suppl 1:S69-S72.
28. Steffen R. Hepatitis A and hepatitis B: risks compared with other vaccine preventable diseases and immunization recommendations. *Vaccine*. 1993;11(5):518-520.
29. Stewart T, Crofts N. An outbreak of hepatitis A among homosexual men in Melbourne. *Med J Aust*. 1993;158(8):519-521.
30. Totos G, Gizaris V, Papaevangelou G. Hepatitis A vaccine: persistence of antibodies 5 years after the first vaccination. *Vaccine*. 1997;15(11):1252-1253.

31. Van Damme P, Mathei C, Thoelen S, Meheus A, Safary A, Andre FE. Single dose inactivated hepatitis A vaccine: rationale and clinical assessment of the safety and immunogenicity. *J Med Virol.* 1994;44(4):435-441.
32. Van Damme P, Thoelen S, Cramm M, De Groote K, Safary A, Meheus A. Inactivated hepatitis A vaccine: reactogenicity, immunogenicity, and long-term antibody persistence. *J Med Virol.* 1994;44(4):446-451.
33. Van Damme P, Thoelen S, Van der Auwera JC Baré, Meheus A. Viral hepatitis among health care workers - epidemiology and prevention. In 1993;(International Congress on Occupational Health):133-137.
34. Van Damme P, Thoelen S Meheus. Long-term immunogenicity of an inactivated hepatitis A vaccine. IX Triennial International Symposium on Viral Hepatitis and Liver Disease. 1996;21-25.
35. Van Damme P, Van Herck K, Thoelen S Meheus. Long-term immunogenicity of an inactivated hepatitis A vaccine. 5th International Conference on Travel Medicine 1997;24-27.
36. Vernon AA, Schable C, Francis D. A large outbreak of hepatitis A in a day-care center: association with non-toilet-trained children and persistence of IgM antibody to hepatitis A virus. *Am J Epidemiol.* 1982;115(3):325-331.
37. WHO. Prevention of foodborne hepatitis A – Considerations on the vaccination of food handlers. WHO Tech Rep Ser. 1993;68:25-26.

PART III: CONSUMER INFORMATION

HAVRIX[®] hepatitis A vaccine, inactivated

This leaflet is part III of a three-part "Product Monograph" published for HAVRIX[®] (hepatitis A vaccine, inactivated) approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about HAVRIX[®]. Contact your doctor or pharmacist if you have any questions about the vaccine.

ABOUT THIS VACCINE

What the vaccine is used for:

HAVRIX[®] is a vaccine used to prevent hepatitis A disease. Vaccination is the best way to protect against this disease.

What it does:

The vaccine works by causing the body to produce its own protection (antibodies) against hepatitis A disease.

When it should not be used:

HAVRIX[®] should not be used:

- if you or your child have a known allergy to any component of the vaccine (see What the important medicinal ingredient is and What the important nonmedicinal ingredients are sections).
- if you or your child have shown signs of a serious allergic reaction after a previous dose of this vaccine or any vaccine intended to protect against hepatitis A infection. Signs of an allergic reaction may include skin rash, shortness of breath and swelling of the face or tongue.

Immunization should be postponed if you or your child has a severe fever or infection.

What the medicinal ingredient is:

The medicinal ingredient in HAVRIX[®] is inactivated hepatitis A virus. None of the components of the vaccine are infectious.

What the important nonmedicinal ingredients are:

HAVRIX[®] contains the following nonmedicinal ingredients: Aluminum hydroxide, amino acids for injection, disodium phosphate, monopotassium phosphate, neomycin sulphate, polysorbate 20, potassium chloride, sodium chloride and water for injection.

What dosage forms it comes in:

HAVRIX[®] is presented as a suspension for injection.

WARNINGS AND PRECAUTIONS

BEFORE you use HAVRIX[®] talk to your doctor or pharmacist if:

- you or your child has a severe infection with a high temperature (over 38°C).
- you or your child have any known allergies.
- you or your child is on dialysis for kidney disease.
- you or your child have a poor immune system due to illness or drug treatment.
- you are pregnant or breast feeding.
- you or your child have a bleeding problem or bruise easily.

Please tell your doctor if you are taking or have recently taken any other medicines. You can be given other vaccines at the same time as HAVRIX[®], however these vaccines will be given at different injection sites.

Fainting can occur following, or even before, any needle injection; therefore, tell the doctor or nurse if you or your child fainted with a previous injection.

INTERACTIONS WITH THIS VACCINE

HAVRIX[®] and immune globulin (human) should be administered at separate injection sites.

When administration of other vaccines with HAVRIX[®] is considered necessary, the vaccines must be given with different syringes and at different injection sites.

PROPER USE OF THIS VACCINE

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Usual dose:

HAVRIX[®] is injected into the muscle in your upper arm or in the front of the thigh in young children.

Primary Immunization:

The first dose of the vaccine should protect you or your child with normal immunity from infection with hepatitis A virus within 2-4 weeks after the injection.

Booster Dose:

To ensure that you or your child are protected long-term you or your child should have a second (booster) dose of the vaccine 6 to 12 months after the first injection.

Missed Dose:

If you or your child miss a scheduled injection, talk to your doctor to arrange another visit.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all vaccines, HAVRIX® can have side effects.

Side effects that may occur are the following:

Very common (more than 10% of doses):

- Irritability.
- Headache.
- Pain and redness at the injection site, fatigue.

Common (between 1% and 10% of doses):

- Loss of appetite.
- Drowsiness.
- Diarrhea, nausea, vomiting.
- Swelling or hard lump at the injection site.
- Generally feeling unwell, fever.

Uncommon (between 0.1% and 1% of doses):

- Upper respiratory tract infection, runny or blocked nose.
- Dizziness.
- Rash.
- Aching muscles, muscular stiffness not caused by exercise.
- Flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills.

If any of the side effects get serious or if you notice any side effects not mentioned above, please tell your doctor.

This is not a complete list of side effects. For any unexpected effects while taking HAVRIX®, contact your doctor or pharmacist.

HOW TO STORE IT

HAVRIX® must be stored in a refrigerator between 2 and 8°C. **Do not freeze.** Discard if the vaccine has been frozen.

Do not use after expiration date shown on the label. The date for last use corresponds to the last day of the month mentioned.

Store all vaccines out of the reach and sight of children.

Store in the original package in order to protect from light.

REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

For health care professionals:

If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in [your province/territory](#).

For the General Public:

Should you experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.

If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada:

By toll-free telephone: 1-866-844-0018

By toll-free fax: 1-866-844-5931

By email: caefi@phac-aspc.gc.ca

At the following website:

<http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php>

By regular mail:

The Public Health Agency of Canada
 Vaccine Safety Section
 130 Colonnade Road
 Ottawa, Ontario
 K1A 0K9 Address Locator 6502A

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.gsk.ca>

or by contacting the sponsor,

GlaxoSmithKline Inc.

7333 Mississauga Road

Mississauga, Ontario

L5N 6L4

1-800-387-7374

This leaflet was prepared by GlaxoSmithKline Inc.

Last revised: July 12, 2011

© 2011 GlaxoSmithKline Inc. All Rights Reserved

® HAVRIX is a registered trademark used under license by GlaxoSmithKline Inc.