Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Havrix Junior Monodose Vaccine. Hepatitis A Vaccine (Inactivated, Adsorbed). 720 ELISA units/ 0.5ml Suspension for injection in a pre-filled syringe

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hepatitis A virus antigen (HM175 strain)*	720 ELISA units/0.5 ml
adsorbed on aluminium hydroxide (adjuvant)	Total: 0.25 mg Al^{3+}

* Produced on MRC-5 human diploid cells

Excipient(s) with known effect:
This vaccine contains phenylalanine 83 micrograms per dose (see section 4.4).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Suspension for injection.
Slightly opaque white suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Havrix Junior Monodose vaccine is indicated for active immunisation against HAV infection in children and adolescents from 1 year up to and including 15 years of age. The vaccine is particularly indicated for those at increased risk of infection or transmission.

4.2 Posology and method of administration

Posology

Children/adolescents (1-15 years)

Primary immunisation
Primary immunisation consists of a single dose of Havrix Junior Monodose vaccine (720 ELISA units/0.5 ml) given intramuscularly.
Havrix Junior Monodose confers protection against hepatitis A within two to three weeks (See Section 5.1, *Pharmacodynamic Effects*).
If exposure to a high risk of contracting hepatitis A is expected within two weeks of the primary immunisation dose, human normal immunoglobulin may be given simultaneously with Havrix Junior Monodose at different injection sites.

Serological data indicate that there should be continuing protection against Hepatitis A for up to 5 years after the first dose of Havrix Junior Vaccine in subjects who responded to the initial vaccination.

Booster Vaccination
After primary vaccination with Havrix Junior Monodose Vaccine, a booster dose is recommended in order to ensure long term protection. This booster dose should be given at any time between 6 months and 5 years, but preferably between 6 and 12 months after the primary dose. (See Section 5.1 *Pharmacodynamic effects*).

Clinical data demonstrate that anti-HAV antibodies persist for at least 10 years in vaccinees who receive the complete vaccination course (i.e. 2 doses of Havrix Junior Monodose Vaccine; See Section 5.1, *Pharmacodynamic effects*).

Method of Administration

Havrix Junior Monodose is for intramuscular use only and must not be given intravascularly. The vaccine should be administered into the deltoid region and not in the gluteal region. Havrix Junior may be injected into the antero-lateral part of the thigh in young children.

Exceptionally the vaccine may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes. However, this route of administration may result in suboptimal response to the vaccine.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 or to neomycin.

Hypersensitivity after previous administration of hepatitis A vaccine.

Havrix Junior Monodose contains less than 10ng traces of neomycin. The vaccine should not be used in subjects with known hypersensitivity to neomycin.

The administration of Havrix Junior Monodose should be postponed in subjects suffering from acute severe febrile illness.

4.4 Special warnings and precautions for use

As with all vaccinations, appropriate medication (e.g. adrenaline) should be readily available for immediate use in case of anaphylaxis.

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.

It is possible that subjects may be in the incubation period of hepatitis A infection at the time of immunisation. It is not known whether Havrix Junior Monodose will prevent hepatitis A in such cases.

In haemodialysis patients and in subjects with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after the primary immunisation and such patients may therefore require administration of additional doses of vaccine.

Excipients

This vaccine contains 83 micrograms of phenylalanine in each dose. Phenylalanine may be harmful to patients that have phenylketonuria (PKU).

This medicine contains potassium, less than 1 mmol (39 mg) per 0.5 ml dose, i.e. essentially 'potassium- free'.

This medicinal product contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, that is to say essentially 'sodium- free'.

4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous administration of Havrix with normal immunoglobulin does not influence the seroconversion rate to Havrix, however it may result in a lower antibody titre. Havrix and immunoglobulins should be administered at separate injection sites.

Preliminary data on the concomitant administration of Havrix, at a dose of 720 ELISA units/ml, with recombinant hepatitis B virus vaccine suggests that there is no interference in the immune response to either antigen. On this basis and since it is an inactivated vaccine, interference with immune response is unlikely to occur when Havrix Junior Monodose is administered with other inactivated or live vaccines.

Havrix Junior Monodose can be given concomitantly with monovalent and combination vaccines comprised of measles, mumps, rubella and varicella.

When concomitant administration is considered necessary the vaccines must be given at different injection sites.

Havrix Junior Monodose must not be mixed with other vaccines in the same syringe.

4.6 Fertility, pregnancy and lactation

Pregnancy
The effect of Havrix Junior Monodose on foetal development has not been assessed. However, as with all inactivated viral vaccines the risks to the foetus are considered to be negligible. Havrix Junior Monodose should be used during pregnancy only when clearly needed.

Breast-feeding
The effect on breast-fed infants of the administration of Havrix Junior Monodose to their mothers has not been evaluated in clinical studies. Havrix Junior Monodose should therefore be used with caution in breast-feeding women.

Fertility
No fertility data are available.

4.7 Effects on ability to drive and use machines

Havrix has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

In controlled clinical studies, the most commonly reported reactions after administration of Havrix Junior Monodose were irritability, headache, pain and redness at the injection site and fatigue.

The safety profile presented below is based on data from more than 5300 subjects.
Frequencies per dose are defined as follows:
Very common: ≥ 1/10
Common: ≥ 1/100 to < 1/10
Uncommon: ≥ 1/1,000 to < 1/100
Rare: ≥ 1/10,000 to < 1/1,000
Very rare: < 1/10,000

- **Clinical trials**

Infections and infestations:
Uncommon: upper respiratory tract infection, rhinitis

Metabolism and nutrition disorders:
Common: appetite lost

Psychiatric disorders:
Very common: irritability

Nervous system disorders:
Very common: headache
Common: drowsiness
Uncommon: dizziness
Rare: hypoaesthesia, paraesthesia

Gastrointestinal disorders:
Common: gastrointestinal symptoms (such as diarrhoea, nausea, vomiting)

Skin and subcutaneous tissue disorders:
Uncommon: rash
Rare: pruritus

Musculoskeletal and connective tissue disorders:

Uncommon: myalgia, musculoskeletal stiffness

General disorders and administration site conditions:
Very common: pain and redness at the injection site, fatigue
Common: malaise, fever (≥37.5°C), injection site reaction (such as swelling and induration)
Uncommon: influenza like illness
Rare: chills

- **Post-marketing surveillance**

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Hepatitis A vaccines, ATC code: J07BC02.

Havrix confers immunisation against Hepatitis A virus (HAV) by stimulating specific immune responses evidenced by the induction of antibodies against HAV.

Immune response
In clinical studies, 99% of vaccinees seroconverted 30 days after the first dose. In a subset of clinical studies where the kinetics of the immune response was studied, early and rapid seroconversion was demonstrated following administration of a single dose of Havrix in 79% of vaccinees at day 13, 85.3% at day 15, 95.2% at day 17 and 100% at day 19, which is shorter than the average incubation period of hepatitis A (4 weeks).

Persistence of the immune response
In order to ensure long term protection, a booster dose should be given between 6 and 12 months after the primary dose of Havrix Vaccine. However, if the booster dose has not been given between 6 and 12 months after the primary dose, the administration of this booster dose can be delayed up to 5 years.

In a comparative trial, a booster dose given up to 5 years after the primary dose has been shown to induce similar antibody levels as a booster dose given between 6 and 12 months after the primary dose.

Long term persistence of hepatitis A antibody titers following 2 doses of Havrix given 6 to 12 months apart has been evaluated. Clinical data demonstrates that a humoral response persists for at least 10 years. Data available after 17 years allows prediction that at least 95% and 90% of subjects will remain seropositive (≥15 mIU/ml) 30 and 40 years after vaccination, respectively (see Table 1).

Table 1: Predicted proportion with anti-HAV level ≥15 mIU/ml and 95% confidence intervals for studies HAV-112 and HAV-123.

Year	≥ 15 mIU/ml	95% CI	
		LL	UL
Predictions for HAV-112			
25	97.69 %	94.22 %	100 %
30	96.53 %	92.49 %	99.42 %
35	94.22 %	89.02 %	98.93 %
40	92.49 %	86.11 %	97.84 %
Predictions for HAV-123			
25	97.22 %	93.52 %	100 %
30	95.37 %	88.89 %	99.07 %
35	92.59 %	86.09 %	97.22 %
40	90.74 %	82.38 %	95.37 %

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

Efficacy of Havrix for outbreak control

The efficacy of Havrix was evaluated in different community-wide outbreaks (Alaska, Slovakia, USA, UK, Israel and Italy). These studies demonstrated that vaccination with Havrix led to termination of the outbreaks. A vaccine coverage of 80% led to termination of the outbreaks within 4 to 8 weeks.

Impact of mass vaccination on disease incidence
A reduction in the incidence of hepatitis A was observed in countries where a two-dose Havrix immunization programme was implemented for children in their second year of life:

- In Israel, two retrospective database studies showed 88% and 95% reduction in hepatitis A incidence in the general population 5 and 8 years after the implementation of the vaccination program, respectively. Data from National Surveillance also showed a 95% reduction in hepatitis A incidence as compared to the pre-vaccination era.
- In Panama, a retrospective database study showed a 90% reduction in reported hepatitis A incidence in the vaccinated population, and 87% in the general population, 3 years after implementation of the vaccination programme.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polysorbate 20, Amino acids for injection (containing phenylalanine), Disodium phosphate anhydrous, Potassium dihydrogen phosphate, Sodium chloride, Potassium chloride, Water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2ºC - 8ºC).
Keep container in the outer carton in order to protect from light.
Do not freeze.
Stability data indicate that Havrix is stable at temperatures up to 25ºC for 3 days. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

6.5 Nature and contents of container

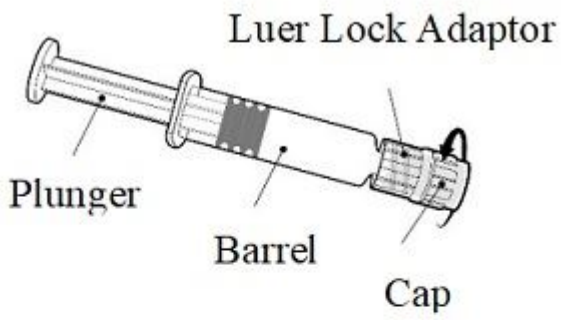
- 0.5 mL of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and with a rubber tip cap.
- 0.5 mL of suspension in a vial (type I glass) with a stopper (butyl rubber).

The tip cap and rubber plunger stopper of the pre-filled syringe and the stopper of the vial are made with synthetic rubber.

6.6 Special precautions for disposal and other handling

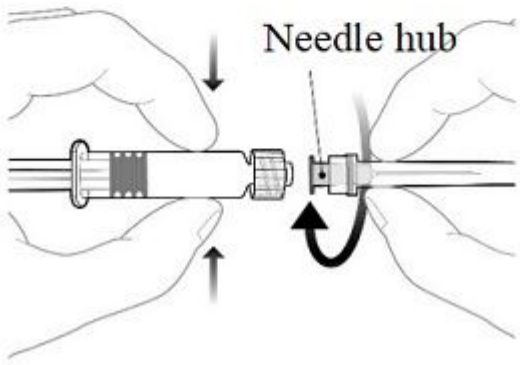
Upon storage, a fine white deposit with a clear colourless supernatant can be observed.
The vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. Before use, the product should be well shaken to obtain a slightly opaque white suspension. Discard if the contents of the syringe appear otherwise.

Instructions for the pre-filled syringe



Hold the syringe by the barrel, not by the plunger.

Unscrew the syringe cap by twisting it anticlockwise.



To attach the needle, connect the hub to the Luer Lock Adaptor and rotate a quarter turn clockwise until you feel it lock.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

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

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1077/026/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02 October 1998

Date of last renewal: 01 October 2008

10 DATE OF REVISION OF THE TEXT

May 2023