AUSTRALIAN PRODUCT INFORMATION

TWINRIX (720/20) AND TWINRIX JUNIOR (360/10) (combined Hepatitis A and Hepatitis B vaccine) suspension for injection

1 NAME OF THE MEDICINE

Combined hepatitis A and hepatitis B vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

TWINRIX is a non-infectious combination vaccine containing hepatitis A virus antigen and hepatitis B surface antigen (rys).

Each 1 mL dose of TWINRIX contains 720 ELISA units of hepatitis A virus antigen and 20 micrograms of hepatitis B surface antigen (rys). The viral antigens are adsorbed on 0.45 mg aluminium in the form of aluminium phosphate and aluminium hydroxide hydrate and suspended in a solution containing 8.8 mg of sodium chloride.

Each 0.5 mL dose of TWINRIX Junior contains 360 ELISA units of hepatitis A virus antigen and 10 micrograms of hepatitis B surface antigen (rys). The viral antigens are adsorbed on 0.225 mg aluminium in the form of aluminium phosphate and aluminium hydroxide hydrate and suspended in a solution containing 4.4 mg of sodium chloride.

TWINRIX is formulated using the HM 175 strain of hepatitis A grown in human cell culture (MRC5), and inactivated with formaldehyde. The hepatitis B surface antigen (rys) component is produced by culturing genetically-engineered *Saccharomyces cerevisiae* yeast cells (Baker's yeast), which carry the relevant gene of an adw subtype, of the surface antigen of the hepatitis B virus. Both the hepatitis A virus antigen and hepatitis B surface antigen (rys) are purified by several physico-chemical steps, and formulated as separate antigen suspensions adsorbed onto aluminium salts. TWINRIX is produced by pooling bulk preparations of the purified antigens. The bulk hepatitis A virus antigen and hepatitis B surface antigen (rys) preparations are identical to those used in the manufacture of the currently licensed monovalent hepatitis A (Havrix) and hepatitis B (Engerix-B) vaccines. Standardised fermentation and purification procedures ensure batch to batch consistency. The vaccines are free of association with human blood or blood products.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

TWINRIX meets the World Health Organization requirements for the manufacture of biological substances.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

TWINRIX is a sterile suspension.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

TWINRIX (720/20) is indicated for active immunisation against hepatitis A and hepatitis B virus infection in adults and children from 1 year of age. TWINRIX Junior (360/10) is indicated for use in children aged 1 to 15 years.

Immunisation against hepatitis A is recommended in the following individuals:

Travellers: Persons travelling to areas of intermediate or high endemicity for hepatitis A. This includes all developing countries.

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.

Persons for whom hepatitis A is an occupational hazard or for whom there is an increased risk of transmission. These include:

- employees in day-care centres particularly in situations where children have not been toilet trained
- teachers and other close contacts of the intellectually disabled
- staff and residents of residential facilities for the intellectually disabled
- healthcare workers and teachers in remote Aboriginal and Torres Strait Islander communities
- nursing staff and other healthcare workers in contact with patients in paediatric wards, infectious diseases wards, emergency rooms and intensive care units
- sewerage workers
- food handlers, since food hygiene procedures and food processing methods are not always adequate to protect from contamination from food handlers

Homosexual men: Increased incidence of hepatitis A infection among homosexual males suggests that the disease may be sexually transmitted in this group.

Contacts of infected persons: Since virus shedding from infected persons may occur for a prolonged period, active immunisation of close contacts is recommended. The use of vaccine in outbreak control has been shown to be more effective than the use of immunoglobulin.

Specific population groups known to have a higher incidence of hepatitis A: eg. Australian Aboriginals, those in settings with recognised community-wide HAV epidemics.

Individuals with chronic liver disease and recipients of liver transplants, as hepatitis A infection is likely to be more severe in these groups. Many injecting drug users will have pre-existing liver disease from hepatitis B or hepatitis C infection.

Recipients of blood products, such as Factor VIII concentrates.

Immunisation against hepatitis B is recommended in the following individuals:

Persons for whom hepatitis B is an occupational hazard or for whom there is an increased risk of transmission. These include:

- healthcare workers directly involved in patient care, or in the handling of human blood or tissue

- embalmers
- staff and residents of residential facilities for the intellectually disabled
- inmates of long term correctional facilities and staff of correctional facilities

Individuals with chronic liver disease and/or hepatitis C.

Haemodialysis patients and recipients of certain blood products such as Factor VIII concentrates.

Sexually active homosexual men and persons with multiple sexual partners: e.g. clients of STD (sexually transmitted disease) clinics. Sexual risk occurs in susceptible (anti-HBs negative) partners of HBV carriers and patients with acute hepatitis B.

Abusers of injectable drugs.

Close residential contacts of deinstitutionalised intellectually disabled individuals who are HBV carriers.

Household contacts of patients with acute hepatitis B and chronic hepatitis B carriers.

Others in whom vaccination against hepatitis B might be justified

Police and members of the armed forces

Travellers to areas of high endemicity for hepatitis B

Participants in contact sports

4.2 DOSE AND METHOD OF ADMINISTRATION

The vaccine should be re-suspended before use. When re-suspended, the vaccine will have a uniform hazy white appearance.

Upon storage, a fine white deposit with a clear colourless layer above may be observed.

Re-suspension of the vaccine to obtain a uniform hazy white suspension

The vaccine can be re-suspended following the steps below.

1. Hold the syringe upright in a closed hand.

2. Shake the syringe by tipping it upside down and back again.

3. Repeat this action vigorously for at least 15 seconds.

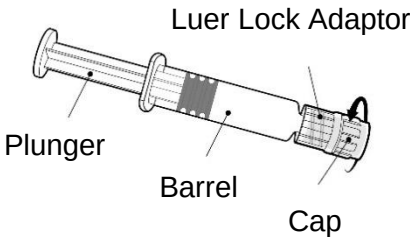
4. Inspect the vaccine again:

    a. If the vaccine appears as a uniform hazy white suspension, it is ready to use - the appearance should not be clear.

    b. If the vaccine still does not appear as a uniform hazy white suspension - tip upside down and back again for at least another 15 seconds - then inspect again.

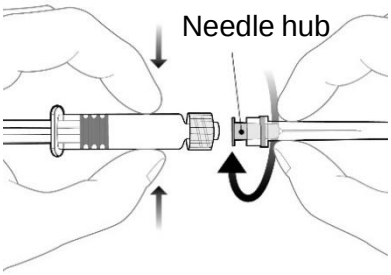
The vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either being observed, do not administer the vaccine.

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.

Each dose of TWINRIX is for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

TWINRIX should be injected intramuscularly into the deltoid region of the upper arm in adults and older children. The antero-lateral aspect of the thigh may be used in infants.

Exceptionally, the vaccine may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders (e.g. haemophiliacs) since bleeding may occur following an intramuscular administration to these subjects. (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

TWINRIX MUST NOT BE GIVEN INTRAVENOUSLY.

IMMUNISATION SCHEDULE

TWINRIX (720/20)

In children and adults not previously exposed to hepatitis A or hepatitis B viruses or vaccines the primary course of TWINRIX is as follows:

TWINRIX (720/20)

Schedule (Course completed in)	Age	Total doses to complete course	Timing:
Standard (6 months)	1-15 years inclusive	2 doses	0, 6 to 12 months

Standard (6 months)	16 years and over	3 doses	0, 1 month, 6 months
Rapid (21 days + 12 months)	16 years and over	4 doses	0, 7 days, 21 days, 12 months

Rapid schedule

The rapid schedule is used in exceptional circumstances in adults when more rapid protection is required, e.g. in travellers commencing vaccination within one month or more of departure. When this rapid schedule is used, a fourth dose is recommended 12 months after the first dose to ensure adequate protection, as lower seroprotection rates against hepatitis B were observed after the third dose as compared to the standard 0, 1, 6 month schedule (See SECTION 5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials)

TWINRIX Junior (360/10)

In circumstances where a child is at immediate risk of exposure to hepatitis B (e.g. travellers), and did not receive a primary course of hepatitis B vaccine as an infant, TWINRIX Junior should be used as follows:

TWINRIX Junior (360/10)

Schedule (Course completed in)	Age	Total doses to complete course	Timing:
Standard (6 months)	1-15 years inclusive	3 doses	0, 1 month, 6 months

Booster dose

Long term clinical studies have demonstrated persistence of anti-HAV and anti-HBs antibodies 20 years after immunisation with TWINRIX (720/20) and 15 years after immunisation with TWINRIX Junior (360/10). As persistence of antibodies were similar to those following the monovalent vaccines, general guidelines for booster vaccination can therefore be drawn from those for the monovalent vaccines.

Hepatitis B.

The need for a booster dose in healthy individuals who have received a full primary vaccination course has not been established. Thus a booster dose is not recommended in these circumstances. Booster doses are recommended for haemodialysis patients and other immunocompromised patients. Refer to the Australian Immunisation Handbook for further guidance.

Hepatitis A. Data available from clinical studies using hepatitis A vaccine (Havrix) show persistence of antibodies after 8 years which is consistent with a projected 20 years persistence (based on mathematical calculations). Further long term follow-up of immunised cohorts will be required to determine the duration of protection following hepatitis A immunisation and whether and when booster doses may be required.

In situations where a booster dose of both hepatitis A and hepatitis B are desired, the combined vaccine can be given. Alternatively, subjects primed with TWINRIX may be administered a booster dose of either of the monovalent vaccines.

4.3 CONTRAINDICATIONS

TWINRIX should not be administered to subjects with known hypersensitivity to any component of the vaccine (e.g. neomycin sulphate), or to subjects having shown signs of hypersensitivity after previous administration of these combined vaccines or the monovalent hepatitis A or hepatitis B vaccines.

As for any vaccine, TWINRIX should not be administered to subjects suffering from acute severe febrile illness. However, the presence of minor infection does not contraindicate vaccination.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

TWINRIX should never be administered intravenously.

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.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of anaphylactic reactions following the administration of the vaccine.

TWINRIX should not be administered in the gluteal region. It should not be routinely administered intradermally, or subcutaneously since these routes of administration may not result in an optimum immune response.

TWINRIX should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. (see SECTION 4.2 DOSE AND METHOD OF ADMINISTRATION)

In elderly subjects, haemodialysis patients and persons with an impaired immune system, adequate anti-HAV and anti-HBs antibody titres may not be obtained after a primary vaccination course. The monitoring of antibody titres and if appropriate the need for additional doses of the appropriate vaccine should be considered in such patients. The rapid schedule has not been studied and is not recommended in such patients.

Caution should be exercised in administering TWINRIX to patients in whom a systemic reaction due to the vaccine may pose a significant risk e.g. in patients with severely compromised cardiopulmonary function.

It is possible that subjects may be in the incubation period of a hepatitis A or hepatitis B infection at the time of vaccination. It is not known whether TWINRIX will prevent hepatitis A and hepatitis B in such cases. These vaccines will not induce the production of anti-HBs antibodies in hepatitis B carriers.

The vaccines will not protect against infection caused by hepatitis C or hepatitis E viruses, or other pathogens known to infect the liver.

Use in renal impairment

See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE statement regarding use in haemodialysis patients.

Use in the elderly

See SECTION 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Paediatric use

See SECTION 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Clinical studies have demonstrated that TWINRIX can be administered concomitantly with diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis, *Haemophilus influenzae* type b and measles-mumps-rubella vaccines. In these trials, the injectable vaccines were given at a different injection site to TWINRIX.

Guidance for co-administration of Twinrix Junior and Cervarix should be drawn from those individual vaccines.

TWINRIX Junior (360/10) can be given concomitantly with Human Papillomavirus (HPV) vaccine (CERVARIX). Administration of TWINRIX Junior (360/10) at the same time as Cervarix (HPV vaccine) has shown no clinically relevant interference in the antibody response to the HPV and hepatitis A antigens. Anti-HBs geometric mean antibody concentrations were lower on co-administration, but the clinical significance of this observation is not known since the seroprotection rates remain unaffected. The proportion of subjects reaching anti-HBs ≥10 mIU/ml was 98.3% for concomitant vaccination and 100% for TWINRIX Junior (360/10) alone. The Product Information documents for TWINRIX Junior and CERVARIX should be consulted for guidance with respect to appropriate usage, population and dosing guidelines for these vaccines.

The concomitant administration of TWINRIX with other vaccines (e.g. pneumococcal, influenza) given at separate sites using separate syringes has not been specifically studied.

TWINRIX must not be mixed with other vaccines in the same syringe.

As with other vaccines, it may be expected that patients receiving immunosuppressive therapy or patients with an immunodeficiency, may not achieve an adequate immune response. (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

Concomitant administration of Normal Human Immunoglobulin with the first dose of hepatitis A vaccine does not influence the seroconversion rate, but may result in a relatively lower anti-HAV antibody titre than when the primary course of vaccine is given alone. TWINRIX and Normal Human Immunoglobulin should be administered at separate injection sites.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

See Section 4.6 FERTILITY, PREGNANCY AND LACTATION, Use in pregnancy

Use in pregnancy

(Pregnancy Category B2)

TWINRIX should be used during pregnancy only when clearly needed, and when the possible advantages outweigh the possible risks for the foetus.

The effect of TWINRIX on embryo-foetal, peri-natal and post-natal survival and development has not been prospectively evaluated in clinical trials.

The effect of TWINRIX on embryo-foetal, peri-natal and post-natal survival and development has been assessed in a study in rats. There were no direct or indirect harmful effects with respect to fertility, pregnancy, embryonal/foetal development, parturition or post-natal development, at 1/5 the adult human dose (9 times greater than the clinical adult exposure based on mg/m^2).

Use in lactation

Adequate human data on use during lactation and adequate animal reproduction studies are not available.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trial Data

The safety profile presented below is based on data from more than 6,000 subjects who received either the standard 0, 1, 6 month schedule or the accelerated 0, 7, 21 days schedule of TWINRIX (720/20).

Events are listed within body systems and categorised by frequency according to the following definitions:

Very common:	≥ 1/10
Common:	≥ 1/100 and < 1/10
Uncommon:	≥ 1/1000 and < 1/100
Rare:	≥ 1/10000 and < 1/1000
Very rare:	< 1/10000

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

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

Infections and infestations: *Common*: viral infection; *Uncommon:* upper respiratory tract infection

Blood and lymphatic system disorders: *Rare*: lymphadenopathy

Metabolism and nutrition disorders: *Rare*: decreased appetite

Nervous system disorders: *Very common*: headache; *Uncommon:* dizziness; *Rare*: hypoaesthesia, paraesthesia

Vascular disorders: *Rare*: hypotension

Skin and subcutaneous tissue disorders: *Rare*: rash, pruritus; *Very rare*: urticaria

Musculoskeletal and connective tissue disorders: *Uncommon*: myalgia; *Rare*: arthralgia

In a clinical trial where TWINRIX was administered at 0, 7, 21 days, solicited general symptoms were reported with the same categories of frequency as defined above. After a fourth dose given at month 12, the incidence of systemic adverse reactions was comparable to that seen after vaccination at 0, 7, 21 days.

During clinical studies with TWINRIX Junior (360/10) (n=538 doses of vaccines administered) the frequency of local reactions in children, although still considered common, were almost half that reported with TWINRIX (720/20) in adults. Of the general reactions reported in these children, most were reported at a similar frequency to TWINRIX (720/20) in adults except upper respiratory tract infection, fever and vomiting which were commonly reported at frequencies of 9.3%, 3.7% and 1.9% respectively.

Other adverse events observed in clinical trials performed with TWINRIX Junior include:

Blood and lymphatic system disorders: *Rare*: lymphadenopathy

Metabolism and nutrition disorders: *Common*: appetite lost

General disorders and administration site conditions: *Very common*: pain and redness at the injection site; *Common*: irritability, swelling at the injection site, injection site reaction, fatigue, malaise, fever (≥ 37.5˚C)

Nervous system disorders: *Common*: drowsiness, headache; *Rare*: dizziness

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

Skin and subcutaneous tissue disorders: *Uncommon*: rash; *Rare*: urticaria

In a comparative trial in children and adolescents, *(n = 745 doses)* the percentage of subjects reporting solicited adverse events after a primary course of TWINRIX (720/20) used in a two dose schedule was similar to that seen with TWINRIX Junior (360/10) given in a 3 dose schedule. Pain was reported in 50.7% of the Twinrix (720/20) group and in 39.1% of the TWINRIX Junior (360/10) group. Incidence of redness was 16.1% and 11.9% and swelling was reported in 4.4% and 4.9% in the TWINRIX and TWINRIX Junior groups respectively.

General reactions solicited in controlled clinical trials that may occur in temporal association with TWINRIX used in a two dose schedule in children and adolescents include:

General disorders and administration site conditions: *Very rare*: influenza like illness, chills

Nervous system disorders: *Very rare*: hypoaesthesia, paraesthesia

Gastrointestinal disorders: *Common*: gastrointestinal symptoms (such as diarrhoea)

Musculoskeletal and connective tissue disorders: *Very rare*: myalgia, arthralgia

Skin and subcutaneous tissue disorders: *Very rare*: pruritus

Vascular disorders: *Very rare*: hypotension

Post Marketing Data

The following adverse reactions have been reported with either TWINRIX or with monovalent hepatitis A or B vaccines

Infections and infestations: Meningitis

Blood and lymphatic system disorders: Thrombocytopenia, thrombocytopenic purpura

Immune system disorders: Anaphylaxis, allergic reactions including anaphylactoid reactions and mimicking serum sickness

Nervous system disorders: Encephalitis, encephalopathy, neuritis, neuropathy, paralysis, convulsions

Vascular disorders: Vasculitis

Skin and subcutaneous tissue disorders: Angioneurotic oedema, lichen planus, erythema multiforme

Musculoskeletal and connective tissue disorders: Arthritis, muscular weakness

General disorders and administration site conditions: Immediate injection site pain, stinging and burning sensation

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

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.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

TWINRIX induces the production of specific anti-HAV and anti-HBs antibodies, which confer immunity against HAV and HBV infection.

Clinical trials

Adults – Standard schedule

The immunogenicity of TWINRIX (720/20) has been investigated using a 0, 1 and 6 month vaccination schedule in randomised clinical studies involving over 700 adult volunteers.

Specific humoral antibodies (seropositivity) against HAV were elicited in**:**

- 92-96% of vaccines one month after the first dose
- 97-100% of vaccines one month after the second dose
- 100% of vaccines one month after the third dose.

Seropositivity was defined as anti-HAV antibody titres ≥ 33 IU/L.

Seroprotective levels of anti-HBs antibodies (titers ≥10 IU/L) were elicited in:

- 33.7% of vaccines one month after the first dose
- 83.9% of vaccines one month after the second dose
- 99.3% of vaccines one month after the third dose.

An anti-HBs antibody titre above 10 IU/L correlates with protection against hepatitis B infection.

Adults- Rapid Schedule

The immunogenicity of TWINRIX (720/20) has also been investigated using a 0, 7, 21 day primary schedule plus a fourth dose at month 12 in a randomised clinical study involving over 400 adult volunteers, of whom 239 received TWINRIX (720/20).

Specific humoral antibodies (seropositivity) against HAV were elicited in**:**

- 100% of vaccines one week after the third dose
- 99.5% of vaccines five weeks after the third dose
- 100% of vaccines one month after the fourth dose.

Seroprotective levels of anti-HBs antibodies (titers ≥10 IU/L) were elicited in:

- 82% of vaccines one week after the third dose
- 85% of vaccines five weeks after the third dose
- 100% of vaccines one month after the fourth dose.

Children

The immunogenicity of TWINRIX (720/20) has been investigated using a 0 and 6 month vaccination schedule in randomised clinical studies involving 451 subjects aged 1 to 15 years old.

Specific humoral antibodies (seropositivity) against HAV were elicited in:

- 99.1% of vaccines one month after the first dose
- 100% of vaccines one month after the second dose.

Seroprotective levels of anti-HBs antibodies (titers ≥10 IU/L) were elicited in:

- 37.4% of vaccines one month after the first dose

- 70.5% of vaccines 6 months after the first dose
- 98.2% of vaccines one month after the second dose.

In a clinical study involving 117 subjects who received the second dose at month 12, specific humoral antibodies (seropositivity) against HAV were elicited in 99.0% of vaccines one month after the second dose, and seroprotective levels of anti-HBs were induced in 97.0% of subjects.

The immunogenicity of TWINRIX Junior (360/10) has been investigated using a 0, 1 and 6 month vaccination schedule in randomised clinical studies involving 168 children: 54 subjects aged 1 to 6 years and 114 subjects aged 6 to 15 years.

Specific humoral antibodies (seropositivity) against HAV were elicited in:

- 100% of vaccines one month after the second dose
- 100% of vaccines one month after the third dose.

Seroprotective levels of anti-HBs antibodies (titers ≥10 IU/L) were elicited in:

- 86.2% to 94.6% of vaccines one month after the second dose
- 100% of vaccines one month after the third dose.

In a comparative study in children and adolescents, TWINRIX (720/20) following a 0 and 6 month schedule was proven to be non-inferior for both hepatitis A and B antibody responses to TWINRIX Junior (360/10) following a 0, 1 and 6 month schedule. However, seroprotection rates for hepatitis B at month 2 after two doses of TWINRIX Junior (given one month apart) were higher (85.6%) than after a single dose of TWINRIX (38.0%).

Antibody Persistence

TWINRIX Junior (360/10)

In two long term clinical studies, persistence of anti-HAV and anti-HBs antibodies has been demonstrated up to 15 years in children aged 12-15 years and up to 5 years in children aged 1-11 years. For 1-11 years age cohort, after the primary vaccination with 0, 1, 6 month schedule of TWINRIX Junior, all subjects followed up to 5 years (N=102) retained ≥15 mIU/mL anti-HAV antibody and 97% retained anti-HBs antíbody ≥10 mIU/mL. For 12-15 years age cohort, after the primary vaccination with 0, 1, 6 month schedule of TWINRIX Junior, all subjects followed up to 15 years (N=102) retained ≥15 mIU/mL anti-HAV antibody and 81.8% retained anti-HBs antibody ≥10 mIU/mL. A challenge dose of a HBV vaccine was given to a limited number of subjects (n=11) whose anti-HBs antibody concentration decreased to < 10mIU/mL and 90.9% mounted an anamnestic response.

TWINRIX (720/20)

In two long term clinical studies conducted in 43 healthy adults aged 17-43 years, 20 years after the primary vaccination with Twinrix (720/20), the anti-HAV seropositivity rates were 100% and 96% respectively and the anti-HBs seroprotection rates were 94% and 92%, respectively.

In two clinical studies conducted in subjects over 40 years of age, the seropositivity rate for anti-HAV antibodies and seroprotection rate against hepatitis B following Twinrix (720/20) on a 0, 1, 6 month schedule were compared with the seropositivity and seroprotection rates of monovalent hepatitis A and B vaccines when administered separately.

The seroprotection rates against hepatitis B after the administration of Twinrix (720/20) were 92% and 57% at 7 and 48 months following the first dose respectively, versus 80% and 40% after the GlaxoSmithKline Biologicals monovalent 20 µg hepatitis B vaccine, and 71% and 27% after another licensed monovalent 10 µg hepatitis B vaccine. In all groups, anti-HBs antibody concentrations decreased as age and body mass index increased; concentrations were also lower in males compared with females.

The seropositivity rates for anti-HAV antibodies after Twinrix (720/20) were 97% at both 7 and 48 months following the first dose versus 99% and 94% after the GlaxoSmithKline Biologicals monovalent hepatitis A vaccine and 99% and 96% after another licensed monovalent hepatitis A vaccine.

Subjects received an additional dose of Twinrix (720/20) to assess the immune memory 48 months after the first dose of the primary vaccination course with the same vaccine. One month after this dose, 95% of subjects elicited anti-HBV antibody concentration ≥ 10 mIU/ml and Geometric Mean Concentrations (GMC) increased by 179-fold (GMC of 7233.7 mIU/ml) indicative of an immune memory response.

Anti-HAV and anti-HBs antibodies have been shown to persist for at least 24 months following the initiation of a 0, 6 month schedule of TWINRIX (720/20) in children. Specific humoral antibodies (seropositivity) against HAV were elicited in 100% of vaccines at month 24, and anti-HBs seroprotective levels were present in 93.3% of subjects. In this study, the immune response for both antigen components was comparable to that seen after a 3-dose regimen of TWINRIX Junior (360/10).

The persistence of anti-HAV and anti-HBs antibodies at month 24 was shown to be similar following a 0, 6 month or a 0, 12 month schedule of TWINRIX (720/20) in children.

Hepatitis D

As hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection, it can be expected that hepatitis D will also be prevented by vaccination with TWINRIX.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to vaccines.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The vaccine preparation also contains ≤ 0.45 mg/mL aluminium in the form of aluminium phosphate and aluminium hydroxide hydrate suspended in a solution containing ≤ 8.8 mg/mL of sodium chloride, 1 mg/mL of amino acid supplement, < 20 ng/mL of neomycin sulphate, 50 micrograms/mL of polysorbate 20, < 7 micrograms/mL of dibasic sodium

phosphate heptahydrate, < 5 micrograms/mL of monobasic sodium phosphate, < 250 micrograms/mL of trometamol and < 100 micrograms/mL of formaldehyde.

6.2 INCOMPATIBILITIES

See SECTION 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

TWINRIX must be stored between +2°C to +8°C. DO NOT FREEZE; freezing destroys the potency of the product. Discard the vaccine if it has been frozen. Store in the original package in order to protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

TWINRIX:

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

TWINRIX Junior:

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.

The tip cap and rubber plunger stopper of the pre-filled syringe are not made with natural rubber latex.

TWINRIX and TWINRIX Junior are available as a pre-filled syringe in packs of one or ten.

Not all presentations and pack sizes may be marketed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Not relevant to vaccines.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd

Level 4, 436 Johnston Street,

Abbotsford, Victoria, 3067

9 DATE OF FIRST APPROVAL

18 October 2007

10 DATE OF REVISION

12 March 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2	Editorial changes made to provide clarity to the prescriber and update to booster section to align with AIH
4.2, 5.1	Inclusion of additional persistence data

Version 12.0