Package leaflet: Information for the user

Twinrix® Adult, Suspension for injection in pre-filled syringe
Hepatitis A (inactivated) and hepatitis B (rDNA) (HAB) vaccine (adsorbed)

Read all of this leaflet carefully before you start receiving this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This vaccine has been prescribed for you only. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Twinrix Adult is and what it is used for

Twinrix Adult is a vaccine used in adults and adolescents 16 years of age and above to prevent two diseases: hepatitis A and hepatitis B. The vaccine works by causing the body to produce its own protection (antibodies) against these diseases.

- **Hepatitis A:** Hepatitis A is an infectious disease, which can affect the liver. This disease is caused by the hepatitis A virus. The hepatitis A virus can be passed from person to person in food and drink, or by swimming in water contaminated by sewage. Symptoms of hepatitis A begin 3 to 6 weeks after coming into contact with the virus. These consist of nausea (feeling sick), fever and aches and pains. After a few days the whites of eyes and skin may become yellowish (jaundice). The severity and type of symptoms can vary. Young children may not develop jaundice. Most people recover completely but the illness is usually severe enough to keep people ill for about a month.

- **Hepatitis B:** Hepatitis B is caused by the hepatitis B virus. It causes the liver to become swollen (inflamed). The virus is found in body fluids such as blood, semen, vaginal secretions, or saliva (spit) of infected people.

Vaccination is the best way to protect against these diseases. None of the components in the vaccine are infectious.

2. What you need to know before you receive Twinrix Adult

Twinrix Adult should not be given if
- you are allergic to:
  - the active substances or any of the other ingredients of this medicine (listed in section 6).
  - neomycin.

  Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- you have previously had an allergic reaction to any vaccine against hepatitis A and hepatitis B diseases.

- you have a severe infection with a high temperature (over 38°C). A minor infection such as a cold should not be a problem, but talk to your doctor first.

Warnings and precautions
Talk to your doctor or pharmacist before receiving Twinrix Adult if
- you have experienced any health problems after previous administration of a vaccine.
- you have a poor immune system due to illness or drug treatment.
- you have a bleeding problem or bruise easily.

Fainting can occur (mostly in adolescents) following, or even before, any needle injection. Therefore tell the doctor or nurse if you fainted with a previous injection.

A poor response to the vaccine, possibly without achieving protection against hepatitis A, has been observed in obese people. A poor response to the vaccine, possibly without achieving protection against hepatitis B, has also been observed in older people, men rather than women, smokers, obese people, and people with long standing illnesses, or people on some type of drug treatments. Your doctor may advise you to have a blood test after you have completed the course of vaccinations to check if you have made a satisfactory response. If not, your doctor will advise you on the possible need to have extra doses.

Other medicines and Twinrix Adult
Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think that you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you are given this vaccine. It is not known if Twinrix Adult passes into breast milk, however the vaccine is not expected to cause problems in breast-fed babies.

Twinrix Adult contains neomycin
Please tell your doctor if you have had an allergic reaction to neomycin (antibiotic).

3. How Twinrix Adult is given

You will receive a total of three injections over 6 months. Each injection is given on a separate visit. The first dose will be given on an elected date. The remaining two doses will be given one month, and six months after the first dose.

- First dose: at an elected date
- Second dose: 1 month later
- Third dose: 6 months after the first dose

Twinrix Adult can also be given as a total of three doses over 1 month. This schedule may be given to adults only needing a rapid protection (e.g. overseas travellers). The first dose will be given on an elected date. The remaining 2 doses will be given 7 days and 21 days after the first dose. A fourth dose is recommended at 12 months.

- First dose: at an elected date
- Second dose: 7 days later
- Third dose: 21 days after the first dose
- Fourth dose: 12 months after the first dose

Your doctor will advise on the possible need for extra doses, and future booster dosing.

As indicated in section 2, a poor response to the vaccine, possibly without achieving protection against hepatitis B, is more common in older people, men rather than women, smokers, obese people, and people with long standing illnesses, or people on some type of drug treatments. Your doctor may advise you to have a blood test after you have completed the course of vaccinations to check if you have made a satisfactory response. If not, your doctor will advise you on the possible need to have extra doses.

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

Make sure you finish the complete vaccination course of three injections. If not, you may not be fully protected against the diseases.

The doctor will give Twinrix Adult as an injection into your upper arm muscle.

The vaccine should not be given (deep) into the skin or intramuscularly into the buttock because protection may be less.

The vaccine should never be given into a vein.

If you have any further questions on the use of this vaccine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Side effects that may occur are the following:

Very common (These may occur in 1 in 10 doses or more of the vaccine):
- Headache
- Pain and redness at the injection site
- Tiredness

Common (These may occur in up to 1 in 10 doses of the vaccine):
- Diarrhoea, nausea
- Swelling, bruising or itching at the injection site
- Generally feeling unwell

Uncommon (These may occur in up to 1 in 100 doses of the vaccine):
- Dizziness
- Vomiting, stomach pain
- Aching muscles
- Upper respiratory tract infection
- Fever equal to or greater than 37.5°C

Rare (These may occur in up to 1 in 1,000 doses of the vaccine):
- Swollen glands in the neck armpit or groin (lymphadenopathy)
- Loss of skin sensitivity to pain or touch (hypoaesthesia)
- Feeling of pins and needles (paraesthesia)
- Rash, itching
- Joint pain
- Loss of appetite
- Low blood pressure
- Flu-like symptoms such as high temperature, sore throat, runny nose, cough and chills

Very rare (These may occur in up to 1 in 10,000 doses of the vaccine):

Side effects occurred very rarely during clinical studies or routine use of the vaccine or with individual hepatitis A and hepatitis B vaccines include:

- Reduction in blood platelets, which increases risk of bleeding or bruising (thrombocytopenia)
- Purple or red brown spots visible through the skin (thrombocytopenic purpura)
- Swelling or infection of the brain (encephalitis)
- Degenerative disease of the brain (encephalopathy)
- Inflammation of nerves (neuritis)
- Numbness or weakness of the arms and legs (neuropathy), paralysis
- Fits or seizures
- Swelling of the face, mouth or throat (angioneurotic oedema)
- Purple or reddish-purple bumps on the skin (lichen planus), serious skin rashes (erythema multiforme), hives
- Joint swelling, muscular weakness
- Infection around the brain which may give severe headache with stiff neck and sensitivity to light (meningitis)
- Inflammation of some blood vessels (vasculitis)
- Serious allergic reactions (anaphylaxis, anaphylactoid reactions and mimicking serum sickness). Signs of serious allergic reactions may be rashes that may be itchy or blistering, swelling of the eyes and face, difficulty in breathing or swallowing, a sudden drop in blood pressure and loss of consciousness. Such reactions may occur before leaving the doctor's surgery. However, if you get any of these symptoms you should contact a doctor urgently.
- Abnormal laboratory liver test results
- Multiple sclerosis, swelling of the spinal cord (myelitis)
- Drooping eyelid and sagging muscles on one side of the face (facial palsy)
- A temporary inflammation of the nerves, causing pain, weakness and paralysis in the extremities and often progressing to the chest and face (Guillain-Barré syndrome)
- A disease of the nerves of the eye (optic neuritis)
- Immediate injection site pain, stinging and burning feeling

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

Ireland
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2;
Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Twinrix Adult

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).
Store in the original package in order to protect from light.
Do not freeze. Freezing destroys the vaccine.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Twinrix Adult contains

- The active substances are:

Hepatitis A virus (inactivated)[1,2]	720 ELISA Units
Hepatitis B surface antigen[3,4]	20 micrograms

[1]Produced on human diploid (MRC-5) cells
[2]Adsorbed on aluminium hydroxide, hydrated 0.05 milligrams Al^{3+}
[3]Produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[4]Adsorbed on aluminium phosphate 0.4 milligrams Al^{3+}

- The other ingredients in Twinrix Adult are: sodium chloride, water for injections.

What Twinrix Adult looks like and contents of the pack

Suspension for injection in pre-filled syringe.

Twinrix Adult is a white, slightly milky liquid presented in a glass pre-filled syringe (1 ml).

Twinrix Adult is available in packs of 1, 10, and 25 with or without needles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

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

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

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

The vaccine should 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.

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