

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

VAQTA Adult, suspension for injection
Hepatitis A vaccine, inactivated, adsorbed.
For adults.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:

Hepatitis A virus (strain CR 326F) (inactivated) ^{1,2}25 U³

¹ Produced on human diploid (MRC-5) fibroblast cells.

² Adsorbed on amorphous aluminium hydroxyphosphate sulfate (0.225 mg Al³⁺).

³ Units measured according to the in-house method of the manufacturer-Merck Sharp & Dohme LLC.

This vaccine may contain traces of neomycin and formaldehyde, which are used during the manufacturing process. See sections 4.3 and 4.4.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection in a prefilled syringe or vial.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

VAQTA Adult is indicated for active pre-exposure prophylaxis against disease caused by hepatitis A virus. VAQTA Adult is recommended for healthy adults 18 years of age and older who are at risk of contracting or spreading infection or who are at risk of life-threatening disease if infected (e.g., those with Human Immunodeficiency Virus [HIV] or hepatitis C with diagnosed liver disease).

The use of VAQTA Adult should be based on official recommendations.

For optimal antibody response, primary immunisation should be given at least 2, preferably 4, weeks prior to expected exposure to hepatitis A virus.

VAQTA Adult will not prevent hepatitis caused by infectious agents other than hepatitis A virus.

4.2 Posology and method of administration

Posology

The vaccination series consists of one primary dose and one booster dose given according to the following schedule:

Primary dose:

Adults 18 years of age and older should receive a single 1.0 mL (50U) dose of vaccine at an elected date.

Booster dose:

Adults 18 years of age and older who received a primary dose should receive a booster dose of 1.0 mL (50U) 6 to 18 months after the first dose.

Hepatitis A virus (HAV) antibodies persist for at least 6 years after the second dose (i.e. booster). Based on mathematic modeling duration of antibody persistence is predicted for at least 25 years (see section 5.1).

Interchangeability of the booster dose

A booster dose of VAQTA may be given at 6 to 12 months following the initial dose of other inactivated hepatitis A vaccines. (See section 5.1.)

Adults with HIV:

HIV-infected adults should receive a single dose of 1.0mL (50U) of VAQTA Adult at an elected date followed by a booster dose of 1.0mL (50U) 6 months later.

Paediatric population

There is a paediatric formulation available for children and adolescents. For details please refer to the Summary of Product Characteristics for VAQTA Paediatric.

Method of Administration

VAQTA Adult should be injected INTRAMUSCULARLY in the deltoid region. The vaccine should not be administered intradermally since administration by this route may result in a less than optimal response.

For individuals with bleeding disorders who are at risk of haemorrhage following intramuscular injection (e.g. haemophiliacs), this vaccine may be administered subcutaneously (see section 5.1).

Precautions to be taken before handling or administering the medicinal product

For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

History of hypersensitivity to the active substances, to any of the excipients listed in section 6.1, to neomycin or to formaldehyde (which may be present as trace residues, see sections 2 and 4.4).

Vaccination should be delayed in subjects with current severe febrile infections.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Individuals who develop symptoms suggestive of hypersensitivity after an injection of VAQTA Adult should not receive further injections of the vaccine. This vaccine may contain traces of neomycin and formaldehyde which are used during the manufacturing process (see sections 2 and 4.3).

VAQTA Adult must not be administered into a blood vessel.

Use caution when vaccinating latex-sensitive individuals using the single dose vial since the vial stopper contains dry natural latex rubber that may cause allergic reactions.

Qualitative testing for antibodies to hepatitis A prior to immunisation should be considered based on the probability of previous hepatitis A virus infection in patients who grew up in areas of high endemicity, and/or with a history of jaundice.

VAQTA Adult does not cause immediate protection against hepatitis A, and there may be a period of 2 to 4 weeks before antibody becomes detectable.

VAQTA Adult will not prevent hepatitis caused by infectious agents other than hepatitis A virus. Because of the long incubation period (approximately 20 to 50 days) for hepatitis A, it is possible for unrecognised hepatitis A infection to be present at the time the vaccine is given. The vaccine may not prevent hepatitis A in such individuals.

As with any vaccine, adequate treatment provisions, including epinephrine (adrenaline), should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

VAQTA Adult may be administered subcutaneously when clinically appropriate (e.g. for people with bleeding disorders who are at risk of haemorrhage), although the kinetics of seroconversion are slower for the first subcutaneous dose of VAQTA Adult compared with historical data for intramuscular administration.

As with any vaccine, vaccination with VAQTA Adult may not result in a protective response in all susceptible vaccinees.

Excipient(s) with known effect:

This medicinal product contains less than 1 mmol (23 mg) sodium per dose and is considered to be essentially sodium free.

4.5 Interaction with other medicinal products and other forms of interaction

If VAQTA Adult is used in individuals with malignancies or those receiving immunosuppressive therapy or who are otherwise immunocompromised, the expected immune response may not be obtained.

Known or presumed exposure to HAV/Travel to endemic areas

Use with immune globulin

For individuals requiring either post-exposure prophylaxis or combined immediate and longer term protection (e.g., travellers departing on short notice to endemic areas), in countries where IG is available VAQTA Adult may be administered concomitantly with IG using separate sites and syringes. Although the antibody titre obtained is likely to be lower than when the vaccine is given alone. The clinical relevance of this observation has not been established.

Use with other vaccines

VAQTA Adult may be given concomitantly at separate injection sites with yellow fever and polysaccharide typhoid vaccines (see section 5.1). Though data in subjects 18 years of age and older are not available, studies in children 12 through 23 months of age have shown that VAQTA may be administered concomitantly with measles, mumps, rubella, varicella, pneumococcal 7-valent conjugate and inactivated polio vaccines. Immunogenicity data are insufficient to support concomitant administration of VAQTA with DTaP (Diphtheria, Tetanus and acellular Pertussis) vaccine.

Interaction studies other than with yellow fever and polysaccharide typhoid vaccines are not yet available; however, interactions with other vaccines are not anticipated when vaccines are administered at different injection sites. When concurrent administration is necessary, VAQTA Adult must not be mixed with other vaccines in the same syringe, and other vaccines should be administered at different sites.

4.6 Fertility, Pregnancy and lactation

Pregnancy

It is not known whether VAQTA Adult can cause foetal harm when administered to a pregnant woman, or can affect reproduction capacity. VAQTA Adult is not recommended in pregnancy unless there is a high risk of hepatitis A infection, and the attending physician judges that the possible benefits of vaccination outweigh the risks to the foetus.

Breast-feeding

It is not known whether VAQTA Adult is excreted in human milk, and the effect on breastfed infants following administration of VAQTA Adult to mothers has not been studied. Hence, VAQTA Adult should be used with caution in women who are breastfeeding.

Fertility

VAQTA Adult has not been evaluated in fertility studies.

Animal reproduction studies have not been conducted with VAQTA Adult.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, VAQTA Adult is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

In clinical trials with 1,529 healthy adults who received one or more doses of hepatitis A vaccine, subjects were followed for elevated temperature and local reactions during a 5-day period postvaccination and systemic adverse events including fever during a 14-day period postvaccination. Injection-site reactions, generally mild and transient, were the most frequently reported adverse events.

Post-marketing safety study

In a post-marketing safety study, a total of 29,587 individuals ≥ 18 years of age received 1 or 2 doses of VAQTA Adult. There was no serious, vaccine-related, adverse event identified. There was no nonserious, vaccine-related, adverse event resulting in outpatient visits, with the exception of diarrhoea/gastroenteritis in adults at a rate of 0.5%.

Tabulated summary of adverse reactions

The table presents adverse reactions reported as vaccine related observed in clinical trials, and in a post-authorisation safety study and adverse reactions spontaneously reported after use of the marketed vaccine.

Adverse reactions are ranked under headings of frequency using the following convention:

[Very Common ($\geq 1/10$); Common ($\geq 1/100$ to $< 1/10$); Uncommon ($\geq 1/1000$ to $< 1/100$); Rare ($\geq 1/10,000$ to $< 1/1000$); Very Rare ($< 1/10,000$); Not Known (cannot be estimated from the available data)].

System Organ Class	Frequency	Adverse reactions
<i>Infections and infestations</i>	Uncommon	Pharyngitis, Upper respiratory infection
	Rare	Bronchitis, Infectious gastroenteritis
<i>Blood and lymphatic system disorders</i>	Uncommon	Lymphadenopathy
	Not Known	Thrombocytopenia ¹
<i>Metabolism and nutrition disorders</i>	Rare	Anorexia
<i>Psychiatric disorders</i>	Rare	Apathy, Insomnia
<i>Nervous system disorders</i>	Common	Headache
	Uncommon	Dizziness, Paresthesia
	Rare	Somnolence, Migraine, Tremor

	Not Known	Guillain-Barré syndrome ¹
<i>Eye disorders</i>	Rare	Itching eye, Photophobia, Tearing
<i>Ear and labyrinth disorders</i>	Uncommon	Ear pain
	Rare	Vertigo
<i>Vascular disorders</i>	Uncommon	Hot flashes
<i>Respiratory, thoracic and mediastinal disorders</i>	Uncommon	Respiratory congestion, Nasal congestion, Cough
	Rare	Pharyngeal edema, Sinus disorder
<i>Gastrointestinal disorders</i>	Uncommon	Nausea, Diarrhoea/ Gastroenteritis ² , Flatulence, Vomiting
	Rare	Dry mouth, Mouth ulcer
<i>Skin and subcutaneous tissue disorders</i>	Uncommon	Pruritus, Urticaria, Erythema
	Rare	Night sweats, Rash, Skin disorder
<i>Musculoskeletal and connective tissue disorders</i>	Common	Arm pain (in the injected arm)
	Uncommon	Myalgia, Stiffness, Shoulder pain, Musculoskeletal pain, Back pain, Arthralgia, Leg pain, Neck pain, Muscle weakness
	Rare	Muscle cramp, Elbow pain, Hip pain, Jaw pain, Spasm
<i>Reproductive system and breast disorders</i>	Rare	Menstruation disorder
<i>General disorders and administrative site conditions</i>	Very Common	Injection-site tenderness, Pain, Warmth, Swelling, Erythema
	Common	Asthenia/Fatigue, Fever ($\geq 38.3^{\circ}\text{C}$, Oral) Injection-site

		ecchymosis, Pain/Soreness
	Uncommon	Injection-site pruritus, Stiffness/Tightness, Pain, Injection-site hematoma, Chills, Abdominal pain, Malaise, Injection-site induration and numbness, Cold sensation, Flu-like illness
	Rare	Injection-site burning, Induration (≤ 2.5 centimeters), Muscle twitching, Rash, Abdominal distention, Chest pain, Flank pain, Irritability

¹ Spontaneous reporting after use of marketed vaccine

² Post-authorisation safety study

Description of selected adverse reactions

As with all vaccines, allergic reactions, in rare cases leading to shock, may occur (see section 4.4).

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There are no data with regard to overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: viral vaccines, hepatitis A, inactivated, whole virus

ATC code: J07BC02

VAQTA Adult contains inactivated virus of a strain which was originally derived by further serial passage of a proven attenuated strain. The virus is grown, harvested, highly purified, formalin inactivated, and then adsorbed onto amorphous aluminium hydroxyphosphate sulfate.

Mechanism of action

Hepatitis A vaccine elicits circulating neutralising antibodies to Hepatitis A virus sufficient to confer protection against the virus.

Clinical efficacy and safety

Clinical studies showed seroconversion rates were 95% in adults within 4 weeks after the recommended primary dose. In a sub-set of these individuals ≥ 60 years of age, data indicate that 88% (n=64) seroconverted by week 4 after the primary dose.

In adults, seropositivity has been shown to persist up to 18 months after a single 50U dose. Persistence of immunologic memory was demonstrated with a substantial anamnestic antibody response to a booster dose of 50U given 6 to 18 months after the primary dose to adults. The data regarding the subjects more than 60 years of age are limited.

Antibody persistence

In studies of healthy adults (18 to 41 years of age) who received an initial 50U dose of VAQTA at Day 0 and a subsequent 50U dose 6 months later, the hepatitis A antibody response to date has been shown to persist to at least 6 years. After an initial decline over 2 years, the GMTs appeared to plateau during the 2 to 6 year period.

Data available from long-term studies up to 10 years on the persistence of HAV antibodies after 2 doses of VAQTA in healthy, immunocompetent subjects up to 41 years of age allows prediction that based on mathematical modelling at least 99% of subjects will remain seropositive (≥ 10 mIU anti-HAV/ml) at least 25 years after vaccination.

Based on this analysis, an additional vaccination following complete primary immunisation with 2 doses appears to be unnecessary. However, decisions regarding additional vaccination should be based on risk-benefit for the individual.

Interchangeability of the booster dose

A clinical study in 537 healthy adults, 18 to 83 years of age, evaluated the immune response to a booster dose of VAQTA Adult and a comparable licensed inactivated hepatitis A vaccine given at 6 or 12 months following initial dose of the comparator vaccine. When VAQTA Adult was given as a booster dose in this case it produced an equivalent immune response and was generally well tolerated. (See section 4.2.)

Concomitant use with immunoglobulin

Concurrent administration to healthy adults (18 to 39 years of age) of 50 U/1.0 mL of VAQTA Adult with immunoglobulin (IG, 0.06 mL/kg) was evaluated in a clinical study. The seroconversion rate at week 24 in the vaccine alone group (97%) was higher than in the vaccine plus IG group (92% $p = 0.050$) but rose to 100% in both groups one month post booster.

Concomitant use with other vaccines

A controlled clinical study was conducted with 240 healthy adults, 18 to 54 years of age, who were randomised to receive either

- VAQTA Adult, yellow fever and polysaccharide typhoid vaccines concomitantly at separate injection sites or
- yellow fever and polysaccharide typhoid vaccines concomitantly at separate injection sites or
- VAQTA Adult alone.

The seropositivity rate (SPR) for hepatitis A when VAQTA Adult, yellow fever and polysaccharide typhoid vaccines were administered concomitantly was generally similar to when VAQTA Adult was given alone. However the GMTs for hepatitis A were reduced when the three vaccines were administered concomitantly. Clinically, this reduction in GMTs may be less relevant compared to the benefits of concomitant administration. The antibody response rates for yellow fever and typhoid were equivalent when yellow fever and polysaccharide typhoid vaccines were administered concomitantly with and without VAQTA Adult. The concomitant administration of these three vaccines at separate injection sites was generally well tolerated. The addition of VAQTA Adult to the standard practice of administering yellow fever and typhoid vaccines does not increase the rates of injection site and systemic adverse reactions. (See section 4.2.)

Subcutaneous administration

In a clinical study with 114 healthy seronegative adults who received subcutaneous administration of VAQTA Adult (50U), at 4 weeks following the first dose, the SPR was 78%, and the GMT was 21 mIU/mL. At 24 weeks following the first dose and just prior to the second subcutaneous injection, the SPR was 95%, and the GMT was 153 mIU/mL. At 4 weeks following the second subcutaneous injection, the SPR was 100%, and the GMT was 1,564 mIU/mL; the GMT was 2,287 mIU/mL in subjects less than 30 years of age compared with a GMT of 1,122 mIU/mL in subjects 30 years of age and older. The kinetics of seropositivity were slower for the first subcutaneous dose of VAQTA Adult compared with historical data for intramuscular administration. At 24 weeks following the first subcutaneous dose, the SPR was similar to the historical data at 4 weeks after the initial intramuscular dose. However, at 4 weeks following the second subcutaneous dose, the SPR was similar to the

historical data 4 weeks after the second dose with intramuscular administration. Subcutaneous administration of VAQTA Adult was generally well tolerated.

Administration in HIV-infected adults

In a clinical study with 180 adults, 60 HIV-positive (20 to 45 years of age) and 90 HIV-negative adults (21 to 53 years of age) received VAQTA Adult (50U) and 30 HIV-positive adults (22 to 45 years of age) received placebo. At 4 weeks following the first dose of VAQTA Adult, the SPR was 61% for HIV-positive adults and 90% for HIV-negative adults. At 28 weeks following the first dose (4 weeks following the second dose) of VAQTA Adult, the SPRs were satisfactory for all groups: 94% (GMT of 1,060 mIU/mL) in HIV-positive and 100% (GMT of 3,602 mIU/mL) in HIV-negative adults. Furthermore, in the HIV-positive group receiving VAQTA Adult, the SPR was 100% (GMT of 1,959 mIU/mL) in subjects with CD4 cell counts ≥ 300 cell/mm³; however, the SPR was 87% (GMT of 517 mIU/mL) in subjects with CD4 cell counts < 300 cell/mm³. Three HIV-positive adults with CD4 cell counts < 100 cells/mm³ did not seroconvert after receipt of 2 doses of vaccine. The kinetics of the immune response were slower in the HIV-positive group compared with the HIV-negative group. There was an increased rate of local and systemic adverse effects reported in HIV-positive versus HIV-negative adults. In HIV-positive adults, administration of VAQTA Adult did not appear to adversely affect the CD4 cell counts and HIV RNA burden.

Post-marketing safety study

In a post-marketing safety study, conducted at a large health maintenance organisation in the United States, a total of 29,587 individuals ≥ 18 years of age received 1 or 2 doses of VAQTA Adult. Safety was monitored by reviewing medical records that tracked emergency room and outpatient visits, hospitalisations and deaths. There was no serious, vaccine-related, adverse event identified among the 29,587 individuals in this study. There was no non-serious, vaccine-related, adverse event resulting in outpatient visits, with the exception of diarrhoea/gastroenteritis in adults at a rate of 0.5%. There was no vaccine-related, adverse event identified that had not been reported in earlier clinical trials with VAQTA Adult.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

No preclinical safety testing was performed using the vaccine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium borate
Sodium chloride
Water for injections

For adjuvant and for information regarding residual components in trace quantities, see sections 2, 4.3 and 4.4.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

DO NOT FREEZE since freezing destroys potency.

6.5 Nature and contents of container

1 mL suspension in a pre-filled syringe (type I glass) with plunger-stopper (bromobutyl).

1 mL suspension in a pre-filled syringe (type I glass) with plunger-stopper (bromobutyl), without needle, with a tip-cap (bromobutyl isoprene blend), with 0, 1 or 2 separate needles.

1 mL suspension in a vial (type I glass), grey rubber stopper (chlorobutyl isoprene blend).

Pack sizes: Pack of 1 syringe or 1 vial.

Not all pack sizes or presentations may be marketed.

6.6 Special precautions for disposal

The vaccine should be used as supplied; no reconstitution is necessary.

Parenteral drug products should be inspected visually for extraneous particulate matter and discoloration prior to administration. After thorough agitation, VAQTA Adult is a slightly opaque white suspension.

Shake well immediately before use. Thorough agitation is necessary to maintain suspension of the vaccine. For syringe without attached needle, hold the syringe barrel and attach the needle by twisting in clockwise direction until the needle fits securely on the syringe.

It is important to use a separate sterile syringe and needle for each individual to prevent transmission of infections from one person to another.

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

7 MARKETING AUTHORISATION HOLDER

Merck Sharp & Dohme (UK) Limited
120 Moorgate
London
EC2M 6UR
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 53095/0007

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
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18/12/2025