

**Registration No.:** 1C 15/55 (NB)

**Importer / Manufacturer:** MSD (Thailand) Ltd. / Merck Sharp & Dohme Corp., West Point, Pennsylvania 19486, USA

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1. NAME OF THE MEDICAL PRODUCT**

VAQTA

[Hepatitis A Vaccine, Purified Inactivated, MSD]

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

N/A

### **3. PHARMACEUTICAL FORM**

Intramuscular injection

### **4. CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

VAQTA is indicated for vaccination against infection caused by hepatitis A virus.

VAQTA<sup>®</sup> is an inactivated whole virus vaccine which has been shown to induce antibody to hepatitis A virus protein.

#### **4.2 Posology and method of administration**

**DO NOT INJECT INTRAVASCULARLY OR INTRADERMALLY**

VAQTA is for intramuscular injection. For adults, adolescents, and children older than 2 years of age, the deltoid muscle is the preferred site for intramuscular injection. For children 12 through 23 months of age, the anterolateral area of the thigh is the preferred site for intramuscular injection. While intramuscular injection results in the best immune response, VAQTA may be administered subcutaneously when clinically appropriate. (See PRECAUTIONS.)

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

#### *Children/Adolescents – 12 Months Through 17 Years of Age*

Individuals 12 months through 17 years of age should receive a single 0.5 mL (~25U) dose of vaccine at elected date and a booster dose of 0.5 mL (~25U) 6 to 18 months later.

#### *Adults*

Adults 18 years of age and older should receive a single 1.0 mL (~50U) dose of vaccine at elected date and a booster dose of 1.0 mL (~50U) 6 to 18 months later.

#### *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.

#### *Use With Other Vaccines*

VAQTA may be given concomitantly with yellow fever, typhoid, measles, mumps, rubella, varicella, pneumococcal 7-valent conjugate, oral or inactivated polio, diphtheria toxoid, tetanus toxoid, acellular pertussis, and *Haemophilus influenzae b* vaccines. Data on concomitant use with other vaccines are limited. (See DRUG INTERACTIONS, *Use With Other Vaccines*.)

Separate injection sites and syringes should be used for concomitant administration of injectable vaccines.

#### *Known or Presumed Exposure to HAV/Travel to Endemic Areas*

#### *Use With Immune Globulin*

VAQTA may be administered concomitantly with IG using separate sites and syringes. The vaccination regimen for VAQTA should be followed as stated above. Consult the manufacturer's product circular for the appropriate dosage of IG. A booster dose of VAQTA should be administered at the appropriate time as outlined above (see DRUG INTERACTIONS).

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

Shake well before withdrawal and use. Thorough agitation is necessary to maintain suspension of the vaccine.

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

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

### **4.3 Contraindication**

Hypersensitivity to any component of the vaccine.

### **4.4 Special warnings and precautions for use**

Individuals who develop symptoms suggestive of hypersensitivity after an injection of VAQTA should not receive further injections of the vaccine (see CONTRAINDICATIONS).

Use caution when vaccinating latex-sensitive individuals since the vial stopper and the syringe plunger stopper and tip cap contain dry natural latex rubber that may cause allergic reactions.

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

VAQTA 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 unrecognized 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, should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

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

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

Any acute infection or febrile illness may be reason for delaying use of VAQTA except when, in the opinion of the physician, withholding the vaccine entails a greater risk.

#### **4.5 Interaction with other medical products and forms of interaction**

##### *Use With Other Vaccines*

VAQTA may be given concomitantly with yellow fever, typhoid, measles, mumps, rubella, varicella, pneumococcal 7-valent conjugate, oral or inactivated polio, diphtheria toxoid, tetanus toxoid, acellular pertussis, and *Haemophilus influenzae b* vaccines. Data on concomitant use with other vaccines are limited. (See DOSAGE AND ADMINISTRATION, *Use With Other Vaccines*.)

Separate injection sites and syringes should be used for concomitant administration of injectable vaccines.

The Advisory Committee on Immunization Practices, (ACIP advises the U.S. Public Health Service on vaccination policy), has stated that limited data from studies conducted among adults indicate that simultaneous administration of hepatitis A vaccine with diphtheria, poliovirus (oral and inactivated), tetanus, oral typhoid, cholera, Japanese encephalitis, rabies, or yellow fever vaccine does not decrease the immune response to either vaccine or increase the frequency of reported adverse events. Studies indicate that hepatitis B vaccine can be administered with VAQTA without affecting immunogenicity or increasing the frequency of adverse events.

##### *Use With Immune Globulin*

For individuals requiring either post exposure prophylaxis or combined immediate and longer-term protection (e.g., travelers departing on short notice to endemic areas), VAQTA may be administered concomitantly with IG using separate sites and syringes.

#### **4.6 Pregnancy and lactation**

##### **PREGNANCY**

Animal reproduction studies have not been conducted with VAQTA. It is also not known whether VAQTA can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. VAQTA should be given to a pregnant woman only if clearly needed.

##### **NURSING MOTHERS**

It is not known whether VAQTA is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VAQTA is administered to a woman who is breast-feeding.

##### **PEDIATRIC USE**

VAQTA has been shown to be generally well tolerated and highly immunogenic in individuals 12 months through 17 years of age. See DOSAGE AND ADMINISTRATION for the recommended dosage schedule.

Safety and effectiveness in infants below 12 months of age have not been established.

#### **4.7 Effects on the ability to drive and use machines**

N/A

#### **4.8 Undesirable effects**

##### *Clinical Studies*

##### **Children – 12 Months Through 23 Months of Age**

In 5 combined clinical trials (Protocols 043, 057, 066, 067, and 068), 4374 children 12 through 23 months of age received one or two ~25U doses of VAQTA. Out of the 4374 children who received VAQTA, 3885 (88.8%) children received 2 doses of VAQTA, with 1250 (32.2%) of those children receiving VAQTA concomitantly with other vaccines. Children were followed for elevated temperature and injection-site adverse reactions during a 5-day period postvaccination and systemic adverse events during a 14-day period postvaccination.

The most frequently reported injection-site adverse reaction after any dose of VAQTA was injection-site pain/tenderness/soreness. The data from three of the five protocols (066, 067, and 068) were combined as these three studies specifically prompted for injection-site erythema, pain/tenderness/soreness, and swelling daily for Day 1 through Day 5 postvaccination whereas Protocols 043 and 057 did not.

The most common systemic adverse events among recipients of VAQTA alone and VAQTA given concomitantly with other vaccines were pyrexia (fever >98.6°F or feverish) and irritability. The rates of all other systemic adverse events were comparable between recipients of VAQTA

alone and VAQTA given concomitantly with other vaccines. The data from the five protocols were combined as similar methods for collecting systemic adverse events were used.

The adverse events that were observed among recipients of VAQTA alone or VAQTA given concomitantly with measles, mumps, rubella, varicella, pneumococcal 7-valent conjugate, oral or inactivated polio, diphtheria toxoid, tetanus toxoid, acellular pertussis, and *Haemophilus influenzae* b vaccines at a frequency of at least 1.0% and regardless of causality, are listed in decreasing order of frequency within each system organ class.

The frequency classifications are as follows:

Very Common ( $\geq 1/10$ ); Common ( $\geq 1/100$ ,  $< 1/10$ )

*Adverse Events in Children 12 Months Through 23 Months of Age Administered VAQTA Alone (At Both Doses)*

*Infections and infestations*

Common: Upper respiratory infection; otitis media; nasopharyngitis; rhinitis; viral infection; croup; gastroenteritis.

*Eye disorders*

Common: Conjunctivitis.

*Respiratory, thoracic and mediastinal disorders*

Common: Rhinorrhea; cough; nasal congestion.

*Gastrointestinal disorders*

Common: Diarrhea; vomiting; teething.

*Skin and subcutaneous tissue disorders*

Common: Dermatitis diaper; rash.

*General disorders and administration site conditions*

Very Common: Injection-site pain/tenderness/soreness; injection-site erythema; pyrexia (fever  $> 98.6^{\circ}\text{F}$  or feverish, Days 1-14); injection-site swelling; irritability.

Common: Fever  $> 102.2^{\circ}\text{F}$ , Oral (Days 1-5); injection-site bruising; injection-site hematoma.

*Adverse Events in Children 12 Months Through 23 Months of Age Administered VAQTA Concomitantly with Measles, Mumps, Rubella, Varicella, Pneumococcal 7-valent Conjugate, Oral or Inactivated Polio, Diphtheria Toxoid, Tetanus Toxoid, Acellular Pertussis, or Haemophilus Influenzae b Vaccines (At Least One Dose)*

*Infections and infestations*

Common: Upper respiratory infection; otitis media; nasopharyngitis; viral infection; otitis; rhinitis; laryngotracheobronchitis.

*Metabolism and nutrition disorders*

Common: Decreased appetite.

*Nervous system disorders*

Common: Crying.

*Eye disorders*

Common: Conjunctivitis.

*Respiratory, thoracic and mediastinal disorders*

Common: Rhinorrhea; cough; nasal congestion; respiratory congestion.

*Gastrointestinal disorders*

Common: Diarrhea; vomiting.

*Skin and subcutaneous tissue disorders*

Common: Rash; dermatitis diaper; measles-like/rubella-like rash.

*General disorders and administration site conditions*

Very Common: Injection-site pain/tenderness/soreness; pyrexia (fever >98.6°F or feverish, Days 1-14); injection-site erythema; injection-site swelling; irritability.

Common: Fever ≥102.2°F, Oral (Days 1-5); injection-site bruising.

**Children/Adolescents – 2 Through 17 Years of Age**

In combined clinical trials involving 2595 healthy children (≥2 years of age) and adolescents (including the Monroe Efficacy Study, a placebo-controlled study of 1037 participants) who received one or more ~25U doses of hepatitis A vaccine, subjects were followed for fever and

local complaints during a 5-day period postvaccination and systemic complaints during a 14-day period postvaccination. Injection-site complaints, generally mild and transient, were the most frequently reported complaints. Listed below are the complaints reported by  $\geq 1\%$  of subjects, without regard to causality, in decreasing order of frequency within each body system.

*LOCALIZED INJECTION-SITE REACTIONS (generally mild and transient)*

Pain (18.7%); tenderness (16.8%); warmth (8.6%); erythema (7.5%); swelling (7.3%); ecchymosis (1.3%).

*BODY AS A WHOLE*

Fever ( $\geq 102^\circ\text{F}$ , Oral) (3.1%); abdominal pain (1.6%).

*DIGESTIVE SYSTEM*

Diarrhea (1.0%); vomiting (1.0%).

*NERVOUS SYSTEM/PSYCHIATRIC*

Headache (2.3%).

*RESPIRATORY SYSTEM*

Pharyngitis (1.5%); upper respiratory infection (1.1%); cough (1.0%).

*LABORATORY FINDINGS*

Very few laboratory abnormalities were reported and included isolated reports of elevated liver function tests, eosinophilia, and increased urine protein.

**Adults – 18 Years of Age and Older**

In combined clinical trials involving 1529 healthy adults who received one or more ~50U doses of hepatitis A vaccine, subjects were followed for fever and local complaints during a 5-day period postvaccination and systemic complaints during a 14-day period postvaccination. Injection-site complaints, generally mild and transient, were the most frequently reported complaints. Listed below are the complaints reported by  $\geq 1\%$  of subjects, without regard to causality, in decreasing order of frequency within each body system.

*LOCALIZED INJECTION-SITE REACTIONS (generally mild and transient)*

Tenderness (52.6%); pain (51.1%); warmth (17.3%); swelling (13.6%); erythema (12.9%); ecchymosis (1.5%); pain/soreness (1.2%).

*BODY AS A WHOLE*

Asthenia/fatigue (3.9%); fever ( $\geq 101^\circ\text{F}$ , Oral) (2.6%); abdominal pain (1.3%).

*DIGESTIVE SYSTEM*

Diarrhea (2.4%); nausea (2.3%).

*MUSCULOSKELETAL SYSTEM*

Myalgia (2.0%); arm pain (1.3%); back pain (1.1%); stiffness (1.0%).

*NERVOUS SYSTEM/PSYCHIATRIC*

Headache (16.1%).

*RESPIRATORY SYSTEM*

Pharyngitis (2.7%); upper respiratory infection (2.8%); nasal congestion (1.1%).

*UROGENITAL SYSTEM*

Menstruation disorder (1.1%).

Local and/or systemic hypersensitivity reactions occurred in <1% of children, adolescents, or adults in clinical trials and included the following regardless of causality: pruritus, urticaria, and rash.

As with any vaccine, there is the possibility that use of VAQTA in very large populations might reveal adverse experiences not observed in clinical trials.

#### *Post-marketing Safety Study*

In a post-marketing safety study, a total of 42,110 individuals  $\geq 2$  years of age received 1 or 2 doses of VAQTA. 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 diarrhea/gastroenteritis in adults at a rate of 0.5%.

#### *Marketed Experience*

The following additional adverse reactions have been reported with use of the marketed vaccine.

#### *NERVOUS SYSTEM*

Very rarely, Guillain-Barré syndrome, cerebellar ataxia.

#### *HEMIC AND LYMPHATIC SYSTEM*

Very rarely, thrombocytopenia.

### **4.9 Overdose**

There are no data with regard to overdose.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

N/A

### **5.2 Pharmacokinetic properties**

N/A

### **5.3 Preclinical safety data**

N/A

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

N/A

### **6.2 Incompatibilities**

N/A

### **6.3 Shelf life**

36 months

### **6.4 Special precautions for storage**

Store vaccine at 2-8°C (36-46°F).

DO NOT FREEZE since freezing destroys potency.

### **6.5 Nature and content of container**

#### **Pediatric / Adolescent**

VAQTA Single Dose Vial (25U/0.5 mL)

VAQTA 5 Single Dose Vials (25U/0.5 mL)

VAQTA 10 Single Dose Vials (25U/0.5 mL)

VAQTA Single Dose Pre-filled Syringe (25U/0.5 mL)

VAQTA 5 Single Dose Pre-filled Syringes (25U/0.5 mL)

#### **Adult**

VAQTA Single Dose Vial (50U/1 mL)

VAQTA 5 Single Dose Vials (50U/1 mL)

VAQTA 10 Single Dose Vials (50U/1 mL)

VAQTA Single Dose Pre-filled Syringe (50U/1 mL)

VAQTA 5 Single Dose Pre-filled Syringes (50U/1 mL)

### **6.6 Special precautions for disposal and other handling**

N/A

## **7. MARKETING AUTHORISATION HOLDER**

MSD (Thailand) LTD.

Bangkok, Thailand

## **8. MARKETING AUTHORISATION NUMBER(S)**

1C 15/55 (NB)

## **9. DATE OF FIRST AUTHORAISATION/RENEWAL OF THE AUTHORISATION**

28-May-2012

## **10. DATE OF REVISION OF THE TEXT**

Jul-2011