נובמבר 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון: VAQTA 25 U/0.5 ML, VAQTA 50U/ML
ווקטה 25 יחידות/0.5 מ"ל, ווקטה 50 יחידות/מ"ל

Dosage Form: SUSPENSION FOR INJECTION
Composition: HEPATITIS A VIRUS ANTIGEN, INACTIVATED

חברת מרק שארפ ודוהם (ישראל-1996) בע"מ (MSD ישראל) מבקשת ליידע על עדכון העלון לרופא של VAQTA.

להלן לשון ההתוויה המאושרת לתכשיר:

VAQTA [Hepatitis A Vaccine, Inactivated] is indicated for the prevention of disease caused by hepatitis A virus (HAV) in persons 12 months of age and older. The primary dose should be given at least 2 weeks prior to expected exposure to HAV.

VAQTA may be administered along with immune globulin (IG) at a separate site with a separate syringe for post-exposure prophylaxis *[see Clinical Studies (14.5)]*.

למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא המאושר על ידי משרד הבריאות.

טקסט מהותי שהתווסף מודגש בקו תחתון.
טקסט מהותי שהוסר מסומן ~~בקו חוצה~~.

עדכונים מהותיים בעלון לרופא:
הפרקים הבאים עברו עידכון:

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4 CONTRAINDICATIONS

Do not administer VAQTA to individuals with a history of immediate and/or severe allergic or hypersensitivity reactions (*e.g.*, anaphylaxis) after a previous dose of any hepatitis A vaccine, or to individuals who have had an anaphylactic reaction to any component of VAQTA, including neomycin *[see Description (11)]*.

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5 WARNINGS AND PRECAUTIONS

5.1 Prevention and Management of Allergic Vaccine Reactions

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~~Have a~~Appropriate medical treatment and supervision must be available to manage possible ~~immediate-type hypersensitivity~~anaphylactic reactions~~, such as anaphylaxis, should an acute reaction occur.~~ following administration of the vaccine [*see Contraindications (4)*].

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5.5 Sodium content

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

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6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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The most common local adverse reactions and systemic adverse events (≥15%) reported in different clinical trials across different age groups when VAQTA was administered alone or concomitantly were:

- Children — 12 through 23 months of age: injection-site pain/tenderness (~~6.8%-42.1~~37%), injection-site erythema (21.2%), ~~and~~ fever (~~12.3%-18.5%~~16.4% when administered alone, and 27.0% when administered concomitantly).
- Children/Adolescents — 2 through 18 years of age: injection-site pain (18.7%) ~~and headache (2.3%)~~
  •Adults — 19 years of age and older: injection-site pain, tenderness, or soreness (67.0%), injection-site warmth (18.2%) and headache (16.1%) ~~(6.1)~~

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Table~~s~~ 5 presents rates of solicited local reactions at the VAQTA injection site and rates of elevated temperatures (≥100.4°F (≥38.0°C) and ≥102.2°F (≥39.0°C)) that occurred within 5 days following each dose of VAQTA and elevated temperatures >98.6°F (>37.0°C) for a total of 14 days after vaccination; occurrences of these events were recorded daily on diary cards. Table 6 presents rates of unsolicited systemic adverse events that occurred within 14 days at ≥5% in any group following each dose of VAQTA.

~~and 6 present injection-site adverse reactions (Days 1 to 5 postvaccination with VAQTA) and systemic adverse events (Days 1 to 14 postvaccination with VAQTA) observed among recipients of VAQTA concomitantly with ProQuad and pneumococcal 7-valent conjugate vaccine and VAQTA administered separately from ProQuad and pneumococcal 7-valent conjugate vaccine at a rate of at least 1% following any dose of VAQTA. Among all subjects, fever (>98.6°F or feverish) was the most common systemic adverse event, and injection-site pain/tenderness was the most common injection-site adverse reaction.~~

~~In the 14 days after vaccination with any dose of VAQTA, the rate of fever (>98.6°F or feverish) was increased in subjects who received VAQTA with ProQuad and pneumococcal 7-valent conjugate vaccine as compared to VAQTA alone {risk difference (20.0% [95% CI: 13.0, 26.8]) and relative risk (2.10 [95% CI: 1.59, 2.79] in post-hoc analysis)}. A difference in rates of fever was noted after Dose 1 of VAQTA with ProQuad and pneumococcal 7-valent conjugate vaccine, but not after Dose 2 of VAQTA with ProQuad. The rates of fever ≥100.4°F and ≥102.2°F in the five days after vaccination were similar in both treatment groups (Table 6).~~

~~In the 28 days after vaccination, the administration of Dose 1 of VAQTA with Dose 1 of ProQuad and Dose 4 of pneumococcal 7-valent conjugate vaccine does not increase incidence rates of fever (>98.6°F or feverish) as compared to when ProQuad is administered with pneumococcal 7-valent conjugate vaccine alone {38.6% and 42.7%, respectively; relative risk (0.9 [95% CI: 0.75, 1.09])} in post-hoc analysis). Similarly, the administration of Dose 2 of VAQTA with Dose 2 of ProQuad does not increase incidence rates of fever (>98.6°F or feverish) as compared to when Dose 2 of ProQuad is administered alone {17.4% and 17.0%, respectively; relative risk (1.02 [95% CI: 0.70, 1.51])}.~~

Table 5
Incidences of ~~Unsolicited and~~ Solicited Local Adverse Reactions ~~Occurring at ≥1%~~ at the VAQTA Injection Site ~~for~~ and Elevated Temperatures Following Each Dose of VAQTA ~~VAQTA~~ in Healthy Children~~Infants~~ 12~~ through~~ 23 Months of Age Receiving VAQTA Alone or Concomitantly With ProQuad and PCV7*

	Dose 1		Dose 2	
Adverse reaction: Days 1-5 unless noted	**VAQTA alone**	**VAQTA + ProQuad + PCV7 concomitantly**	**VAQTA alone**	**VAQTA + ProQuad concomitantly**
Injection site adverse reactions	N=274	N=311	N=251	N=263
Injection site erythema	11.7%	9.6%	12.7%	9.5%
Injection site pain/tenderness	15.3%	20.9%	20.3%	17.5%
Injection site swelling	9.5%	6.8%	7.6%	6.1%
Temperature > 98.6°F or feverish (>37.0°C) (Days 1-14)	12.4%	35.7%	10.8%	10.3%
	N=243	N=285	N=221	N=237
Temperature ≥ 100.4°F (≥38.0°C)	10.3%	16.8%	10%	4.2%
Temperature ≥ 102.2 °F (≥39.0°C)	2.1%	3.5%	2.3%	2.5%

*Pneumococcal 7-valent Conjugate Vaccine
N=number of subjects for whom data are available.

~~Adverse Reaction~~	~~VAQTA alone (N=323)~~	~~VAQTA with ProQuad + PCV7 (N=330)~~
	~~Rate (n/total n)~~	
~~Injection-site erythema†~~	~~17.8% (51/286)~~	~~13.3% (44/330)~~
~~Injection-site pain/tenderness‡~~	~~25.5% (73/286)~~	~~25.8% (85/330)~~
~~Injection-site swelling‡~~	~~13.3% (38/286)~~	~~9.7% (32/330)~~
~~Injection-site bruising‡,§~~	~~2.4% (7/286)~~	~~1.8% (6/330)~~

	Dose 1	Dose 2
Injection-site rash †‡	0.3% (1/286)	1.2% (4/330)

N=Number of subjects enrolled/randomized.
n=Number of subjects in each category.
* PCV7 = Pneumococcal 7-valent conjugate.
† Adverse Reactions at the injection site (VAQTA) Days 1-5 after vaccination.
‡ Unsolicited Reaction.

Table 6
Incidences of Unsolicited and Solicited Systemic Adverse Events by Body System Occurring at ≥51% in Any Group Following Each Dose of VAQTA in Healthy ChildrenInfants 12 through 23 Months of Age ReceivingAfter Any Dose of VAQTA Alone or Concomitantly With ProQuad and PCV7*

	Dose 1		Dose 2	
Adverse Event: Days 1-14	**VAQTA alone**	**VAQTA + ProQuad + PCV7 concomitantly**	**VAQTA alone**	**VAQTA + ProQuad concomitantly**
	N=274	N=311	N=251	N=263
General Disorders and Administration Site Conditions				
Irritability	3.6%	6.1%	2.8%	2.7%
Infections and Infestations				
Upper respiratory tract infection	3.3%	6.1%	4.8%	5.7%
Skin and Subcutaneous Tissue Disorders				
Dermatitis diaper	1.1%	6.1%	2.4%	3.4%

*Pneumococcal 7-valent Conjugate Vaccine ***Body System*** Adverse Event‡	**VAQTA alone (N=323)** Rate (n/total n)	**VAQTA with ProQuad + PCV7 (N=330)**
Eye disorders‡		
Conjunctivitis	1.4% (4/286)	0.9% (3/330)
Gastrointestinal disorders‡		
Diarrhea	2.8% (8/286)	4.8% (16/330)
Vomiting	2.1% (6/286)	3.0% (10/330)
General disorders and administration site conditions‡		
Irritability	5.9% (17/286)	7.3% (24/330)
Fever ≥102.2°F (≥39.0°C) (Days 1-5 postvaccination)§	3.9% (10/257)	5.5% (16/293)
Fever ≥100.4°F (≥38.0°C) (Days 1-5 postvaccination)§	16.7% (43/257)	18.1% (53/293)
Fever >98.6°F or feverish (Days 1-14 postvaccination)¶	18.5% (53/286)	38.2% (126/330)
Infections and infestations‡		
Croup infectious	1.4% (4/286)	0.9% (3/330)
Ear infection	0.3% (1/286)	1.8% (6/330)
Gastroenteritis	1.0% (3/286)	0.9% (3/330)
Gastroenteritis viral	1.0% (3/286)	0.6% (2/330)
Nasopharyngitis	2.4% (7/286)	3.6% (12/330)
Otitis media	5.9% (17/286)	7.6% (25/330)
Otitis media acute	1.0% (3/286)	0.6% (2/330)
Pharyngitis	1.0% (3/286)	0.9% (3/330)
Pharyngitis streptococcal	1.0% (3/286)	0.6% (2/330)
Rhinitis	2.4% (7/286)	2.1% (7/330)
Roseola	0.3% (1/286)	1.5% (5/330)
Upper respiratory tract infection	6.6% (19/286)	10.3% (34/330)
Viral infection	0.3% (1/286)	2.7% (9/330)
Respiratory, thoracic and mediastinal disorders‡		
Cough	3.1% (9/286)	4.5% (15/330)
Nasal congestion	1.0% (3/286)	2.1% (7/330)
Rhinorrhea	3.1% (9/286)	4.8% (16/330)
Skin and subcutaneous tissue disorders‡		
Dermatitis diaper	3.1% (9/286)	7.9% (26/330)
Rash	1.4% (4/286)	3.0% (10/330)
Rash morbilliform	0.3% (1/286)	2.4% (8/330)
Rash vesicular	0.7% (2/286)	1.2% (4/330)

N=Number of subjects enrolled/randomized.
n=Number of subjects in each category.
*PCV7 = Pneumococcal 7-valent conjugate.
‡Following administration of VAQTA either with or without other vaccines.
‡Systemic Adverse Events reported Days 1-14 after vaccination, regardless of causality.
§T≥100.4°F and T≥102.2°F, recorded Days 1-5 after vaccination
¶Risk difference (20.0% [95% CI: 13.0, 26.8]) and relative risk (2.10 [95% CI: 1.59, 2.79]) in post-hoc analysis.

Data presented in Tables 5 through 6 on solicited local reactions, and solicited and unsolicited systemic adverse events with incidence ≥5% following each dose of VAQTA are representative of other clinical trials of VAQTA in children 12 through 23 months of age.

The following additional unsolicited local adverse reactions and systemic adverse events were observed at a common frequency of ≥1% to <10% in any individual clinical study. This listing includes only the adverse reactions not reported elsewhere in the label. These local adverse reactions and systemic adverse events occurred among recipients of VAQTA alone or VAQTA given concomitantly within 14 days following any dose of VAQTA across four clinical studies.

Eye disorders: Conjunctivitis

Gastrointestinal disorders: Constipation; vomiting

General disorders and administration site conditions: Injection-site bruising; injection-site ecchymosis

Infections and infestations: Otitis media; nasopharyngitis; rhinitis; viral infection; croup; pharyngitis streptococcal; laryngotracheobronchitis; viral exanthema; gastroenteritis viral; roseola

Metabolism and nutrition disorders: Anorexia

Psychiatric disorders: Insomnia; crying

Respiratory, thoracic and mediastinal disorders: Cough; nasal congestion; respiratory congestion

Skin and subcutaneous tissue disorders: Rash vesicular; measles-like/rubella-like rash; varicella-like rash; rash morbilliform

Children/Adolescents — 2 Years through 18 Years of Age

In ~~eleven~~11 ~~randomized~~ clinical trials, ~~(including Monroe Efficacy Study participants) involving~~ 2615 healthy children ~~(~~≥2 years through 18 years of age~~) and adolescents who~~ received at least one dose of VAQTA~~hepatitis A vaccine, subjects were followed for fever and local adverse reactions days 1 to 5 and for systemic adverse events 1 to 14 days postvaccination~~. These studies included administration of VAQTA in varying doses and regimens (~~N=404~~1377 children received one or more 25U~~/0.5 mL~~ doses~~), the Monroe Efficacy Study (N=973), and comparison studies for process and formulation changes (N=1238).~~

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~~The most common adverse events/reactions were injection-site reactions reported by 24.3% of subjects. Of all reported injection-site reactions, 99.4% were mild (*i.e.*, easily tolerated with no medical intervention) or moderate (*i.e.*, minimally interfered with usual activity possibly requiring little medical intervention). Listed below in Table 8 are the local adverse reactions and systemic adverse events reported by ≥1% of subjects, in decreasing order of frequency within each body system.~~

~~**Table 8**~~
~~**Incidences of Local Adverse Reactions and Systemic Adverse Events ≥1% in Healthy Children and Adolescents 2 through 18 Years of Age**~~

Body System Adverse Event	VAQTA Alone (N=2615) Rate (n/total n) 95% CI	Placebo (Alum Diluent)* (N=542) Rate (n/total n) 95% CI
Respiratory, thoracic, and mediastinal disorders†		
Pharyngitis	1.5% (40/2609) (1.1%, 2.1%)	0.9% (5/542) (0.3%, 2.1%)
Upper respiratory infection	1.1% (29/2609) (0.8%, 1.6%)	0.0% (0/542) (0.0%, 0.7%)
Cough	1.0% (26/2609) (0.7%, 1.5%)	0.0% (0/542) (0.0%, 0.7%)
Gastrointestinal disorders†		
Abdominal pain	1.6% (42/2609) (1.2%, 2.2%)	0.9% (5/542) (0.3%, 2.1%)
Diarrhea	1.0% (26/2609) (0.7%, 1.5%)	0.0% (0/542) (0.0%, 0.7%)
Vomiting	1.0% (27/2609) (0.7%, 1.5%)	0.2% (1/542) (0.0%, 1.0%)
Nervous system disorders†		
Headache	2.3% (60/2609) (1.8%, 3.0%)	1.1% (6/542) (0.4%, 2.4%)
General disorders and administration site reactions†‡		
Injection-site pain	18.7% (488/2608) (17.2%, 20.3%)	6.4% (34/534) (4.5%, 8.8%)
Injection-site tenderness	16.9% (441/2608) (15.5%, 18.4%)	6.6% (35/534) (4.6%, 9.0%)
Injection-site warmth	8.6% (223/2608) (7.5%, 9.7%)	1.7% (9/534) (0.8%, 3.2%)
Injection-site erythema	7.5% (195/2608) (6.5%, 8.6%)	1.7% (9/534) (0.8%, 3.2%)
Injection-site swelling	7.3% (190/2608) (6.3%, 8.4%)	1.7% (9/534) (0.8%, 3.2%)
Fever (≥102°F, oral)‡	1.1% (28/2591) (0.7%, 1.6%)	0.9% (5/542) (0.3%, 2.1%)
Injection-site ecchymosis	1.3% (35/2608) (0.9%, 1.9%)	0.4% (2/534) (0.1%, 1.4%)

N=Number of subjects enrolled/randomized.
n=Number of subjects in each category.
*Placebo (Alum diluent) = amorphous aluminum hydroxyphosphate sulfate. Data represent adverse events following a single dose of placebo, since they were subsequently unblinded and received vaccine.
†Systemic Adverse Events reported Days 1 to 14 after vaccination, regardless of causality.
‡Adverse Reactions at the injection site (VAQTA) and measured fevers Days 1 to 5 after vaccination

Adults — 19 Years of Age and Older

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In the 14 days after the first dose of VAQTA was given with or without typhoid Vi polysaccharide and yellow fever vaccines, the proportion of subjects with adverse events was similar between recipients of VAQTA given concomitantly with typhoid Vi polysaccharide and yellow fever vaccines compared to recipients of typhoid Vi polysaccharide and yellow fever vaccines, but higher compared to recipients of without VAQTA alone. Listed below are theTable 8 summarizes solicited local adverse reactions and systemic adverse events (Table 9) andsummarizes unsolicited systemic adverse events (Table 10) reported inat ≥5% in adults who received one or two doses of VAQTA alone and for subjects who received VAQTA concomitantly with typhoid Vi polysaccharide and yellow fever vaccines. There were no solicited systemic complaints reported at a rate ≥5%. Fever ≥101°F (≥38.3°C) occurred in 1.3% of subjects in each group.

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Listed below in Table 104 are the local adverse reactions and systemic adverse events reported by ≥15% of subjects, in decreasing order of frequency within each body system.

Table 110
Incidences of Local Adverse Reactions and Systemic Adverse Events ≥15% in Adults 19 Years of Age and Older

Body System Adverse Events	VAQTA (Any Dose) (N=1645) Rate (n/total n) (95% CI)
Nervous system disorders*	n=1641
Headache	16.1% (265/1641) (14.4%, 18.0%)
Gastrointestinal disorders*	
Abdominal pain	1.3% (22/1641) (0.8%, 2.0%)
Diarrhea	2.6% (43/1641) (1.9%, 3.5%)
Nausea	2.4% (40/1641) (1.8%, 3.3%)
Musculoskeletal and connective tissue disorders*	
Myalgia	1.9% (31/1641) (1.3%, 2.7%)
Arm pain	1.5% (25/1641) (1.0%, 2.2%)
Back pain	1.1% (18/1641) (0.7%, 1.7%)
Stiffness	1.0% (17/1641) (0.6%, 1.7%)
Infections and infestations*	
Pharyngitis	2.9% (47/1641) (2.1%, 3.8%)
Upper respiratory infection	2.7% (45/1641) (2.0%, 3.7%)
General disorders and administration site reactions†	n=1640
Injection-site pain/tenderness/soreness	67.0% (1099/1640) (64.6%, 69.3%)
Injection-site warmth	18.2% (298/1640) (16.3%, 20.1%)
Injection-site swelling	14.7% (242/1640) (13.1%, 16.6%)
Injection-site erythema	13.7% (224/1640) (12.0%, 15.4%)
Asthenia/fatigue	4.0% (67/1641) (3.2%, 5.2%)
Injection-site ecchymosis	1.3% (22/1640) (0.8%, 2.0%)
Fever (≥101°F, oral)‡	1.0% (17/1626) (0.6%, 1.7%)
Reproductive system and breast disorders*	
Menstruation disorders	1.0% (17/1641) (0.6%, 1.7%)

N=Number of subjects enrolled/randomized.
n=Number of subjects in each category.
*Systemic Adverse Events reported Days 1 to 14 after vaccination, regardless of causality.
‡Adverse Reactions at the injection site (VAQTA) and measured fever Days 1 to 5 after vaccination.

N=Number of subjects enrolled/randomized.
n=Number of subjects in each category with data available.
Percent=percentage of subjects for whom data are available with adverse event.
*Systemic Adverse Events reported Days 1 to 14 after vaccination, regardless of causality.
†Adverse Reactions at the injection site (VAQTA) and measured fever Days 1 to 5 after vaccination.

The following additional unsolicited systemic adverse events were observed among recipients of VAQTA that occurred within 14 days at a common frequency of ≥1% to <10% following any dose not reported elsewhere in the label. These adverse reactions have been reported across 4 clinical studies.

Musculoskeletal and connective tissue disorders: Back pain; stiffness

Reproductive system and breast disorders: Menstruation disorders

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6.2 Post-Marketing Experience

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Post-Marketing Observational Safety Study

In a post-marketing, ~~short-term~~60-day safety surveillance study, conducted at a large health maintenance organization in the United States, a total of 42,110 individuals ≥2 years of age received 1 or 2 doses of VAQTA (13,735 children/adolescents and 28,375 adult subjects). Safety was passively monitored by electronic search of the automated medical records database for emergency room and outpatient visits, hospitalizations, and deaths. Medical

MSD

charts were reviewed when ~~indicated. There~~an event was ~~no~~considered to be possibly ~~serious,~~ vaccine-related by the investigator. None of the serious adverse ~~reaction~~events identified ~~among the 42,110~~ were assessed as being related to vaccine by the investigator~~recipients in this study~~.

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7 DRUG INTERACTIONS

7.1 Use with Other Vaccines

Do not mix VAQTA with any other vaccine in the same syringe or vial. Use separate injection sites and syringes for each vaccine. Please refer to package inserts of coadministered vaccines.

~~VAQTA may be given concomitantly with measles, mumps, rubella, varicella, and pneumococcal 7-valent conjugate vaccines *[see Adverse Reactions (6.1) and Clinical Studies (14.7)]*.~~

In clinical trials in children, VAQTA was concomitantly administered with one or more of the following US licensed vaccines: Measles, Mumps, and Rubella Virus Vaccine, Live; Varicella Vaccine, Live; Measles, Mumps, Rubella, and Varicella Vaccine, Live; Pneumococcal 7-valent Conjugate Vaccine. Safety and immunogenicity were similar for concomitantly administered vaccines compared to separately administered vaccines.

In clinical trials in adults, VAQTA was~~may be given to adults~~ concomitantly administered with typhoid Vi polysaccharide and yellow fever vaccines *[see Adverse Reactions (6.1) and Clinical Studies (14.2, 14.7)]*. Safety and immunogenicity were similar for concomitantly administered vaccines compared to separately administered vaccines.

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8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes.

There are no adequate and well-controlled studies designed to evaluate VAQTA in pregnant women. Available post-approval data do not suggest an increased risk of miscarriage or major birth defects in women who received VAQTA during pregnancy.

Developmental toxicity studies have not been conducted with VAQTA in animals.

Data

Human Data

Post-approval adverse reactions are reported voluntarily from a population of uncertain size. It is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine.

In prospectively reported spontaneous post-approval reports from 1995 to 2018, 36 women with a known pregnancy outcome were exposed to VAQTA during pregnancy following the last menstrual period. After excluding induced abortions (n=4) and those with exposure in the third trimester (n=2), there were 30 pregnancies with known outcomes with exposures in the first or second trimester. Miscarriage was reported for 3 of 30 (10%) pregnancies. Major birth defects were reported for 1 of 27 (3.7%) live born infants. The rates of miscarriage and major birth defects were consistent with estimated background rates.

~~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.~~

8.2~~3~~ Lactation~~Nursing Mothers~~

Risk Summary

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.~~ Data are not available to assess the effects of VAQTA on the breastfed infant or on milk production/excretion.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VAQTA and any potential adverse effects on the breastfed child from VAQTA or from the underlying maternal condition. For preventive vaccines the underlying condition is susceptibility to disease prevented by the vaccine.

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12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

~~*Hepatitis A Disease*~~

~~Hepatitis A virus is one of several hepatitis viruses that cause a systemic infection with pathology in the liver. The incubation period ranges from approximately 20 to 50 days. The course of the disease following infection ranges from asymptomatic infection to fulminant hepatitis and death.~~

VAQTA has been shown to elicit antibodies to hepatitis A as measured by ELISA.

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14 CLINICAL STUDIES

14.2 Other Clinical Studies

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Children — 12 through 23 Months of Age

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Of children who received only VAQTA at both visits, 100% (n=97) seroconverted after the second dose of VAQTA. ~~This rate was similar to the expected rate of 99% in 2- to 3-year-old children.~~

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14.7 Immune Response to Concomitantly Administered Vaccines

Clinical Studies of VAQTA with M-M-R II, VARIVAX, and DTaP

~~Concomitant administration of routinely administered recommended childhood vaccines with VAQTA was assessed in a study of 617 children. In this study, the immune response to VAQTA (25U) was assessed in 471 children randomized to receive VAQTA with (N=237) or without M-M-R II and VARIVAX (N=234) at 12 months of age. The race distribution of the study subjects who received at least one dose of VAQTA in these studies was as follows: 56.7% Caucasian; 17.5% Hispanic-American; 14.3% African-American; 7.0% Native American; 3.4% other; 0.8% Oriental; 0.2% Asian; and 0.2% Indian. The distribution of subjects by gender was 53.6% male and 46.4% female.~~ In the clinical trial in which children 12 months of age received the first dose of VAQTA concomitantly with M-M-R II and VARIVAX described in Section 14.2, ~~R~~rates of seroprotection to hepatitis A were similar between the two groups who received VAQTA with or without M-M-R II and VARIVAX. Measles, mumps, and rubella immune responses were tested in 241 subjects, 263 subjects, and 270 subjects, respectively. Seropositivity rates were 98.8% [95% CI: 96.4%, 99.7%] for measles, 99.6% [95% CI: 97.9%, 100%] for mumps, and 100% [95% CI: 98.6%, 100%] for rubella, ~~respectively,~~ which were similar to observed historical rates ~~observed~~ (seropositivity rates 99% for all three antigens, with lower bound of the 95% CI >89%) following vaccination with a first dose of M-M-R II in this age group. Data from this study~~on the varicella immune response~~ were insufficient to adequately assess ~~its immunogenicity when~~the immune response to VARIVAX ~~was~~ administered concomitantly with VAQTA. In this same study, ~~immune responses were evaluated in 183 subjects who were administered~~the second dose of VAQTA ~~with (N=86) and without DTaP (N=97)~~ at 18 months of age was given with or without DTaP. Seropositivity rates for diphtheria and tetanus~~. Rates of seroprotection to hepatitis A~~ were similar to those in historical controls. However, data from this study were insufficient to assess the pertussis response of DTaP when administered with VAQTA. Rates of seroprotection to hepatitis A were similar between the two groups who received VAQTA with or without M-M-R II and VARIVAX, and between the two groups who received VAQTA with or without DTaP. ~~However, data are insufficient to assess the immune response of DTaP when administered with VAQTA.~~

Clinical Studies of VAQTA with ProQuad and Pneumococcal 7-valent Conjugate Vaccine
In ~~a~~the clinical trial ~~involving 653 healthy children 12 to 15 months of age, 330 were randomized to receive~~of concomitant use of VAQTA~~,~~ with ProQuad~~,~~ and pneumococcal 7-valent conjugate vaccine ~~concomitantly, and 323 were randomized to receive ProQuad and pneumococcal 7-valent conjugate vaccine concomitantly followed by VAQTA 6 weeks later. The race distribution of the study subjects was as follows: 60.3% Caucasian; 21.6% African-American; 9.5% Hispanic-American; 7.2% other; 1.1% Asian/Pacific; and 0.3% Native American. The distribution of subjects by gender was 50.7% male and 49.3% female.~~ in children 12 to 15 months of age described in Section 14.2, ~~T~~the antibody GMTs for *S. pneumoniae* types 4, 6B, 9V, 14, 18C, 19F, and 23F 6 weeks after vaccination with pneumococcal 7-valent conjugate vaccine administered concomitantly with ProQuad and VAQTA were non-inferior as compared to GMTs observed in the group given pneumococcal 7-valent conjugate vaccine with ProQuad alone (the lower bounds of the 95% CI around the fold-difference for the 7 serotypes excluded 0.5).

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Clinical Studies of VAQTA with Typhoid Vi Polysaccharide Vaccine and Yellow Fever Vaccine, Live Attenuated
In ~~an open-label~~the clinical trial~~, 240 healthy adults 18 to 54 years~~ of ~~age were randomized to receive either~~concomitant use of VAQTA with typhoid Vi polysaccharide and yellow fever vaccines ~~concomitantly (N=80),~~in adults –18-54 years of age described in Section 6.1, the antibody response rates for typhoid Vi polysaccharide and yellow fever were adequate when typhoid Vi polysaccharide and yellow fever vaccines ~~concomitantly (N=80), or VAQTA alone (N=80). Approximately 6 months later, subjects who received VAQTA~~ were administered ~~a booster dose. The race distribution of the study subjects who received VAQTA with or~~ concomitantly with (N=80) and nonconcomitantly without ~~typhoid Vi polysaccharide and yellow fever vaccine was as follows: 78.3% Caucasian; 14.2% Oriental; 3.3% other; 2.1% African-American; 1.7% Indian; 0.4% Hispanic-American. The distribution of subjects by gender was 40.8% male and 59.2% female~~ VAQTA (N=80). The seropositivity rate for hepatitis A when VAQTA, typhoid Vi polysaccharide, and yellow fever vaccines were administered concomitantly was generally similar to when VAQTA was given alone~~. The antibody response rates for typhoid Vi polysaccharide and yellow fever were adequate when typhoid Vi polysaccharide and yellow fever vaccines were administered concomitantly with and without VAQTA. The GMTs for hepatitis A when VAQTA, typhoid Vi polysaccharide, and yellow fever vaccines were administered concomitantly were reduced when compared to VAQTA alone. Following receipt of the booster dose of VAQTA, the GMTs for hepatitis A in these two groups were observed to be comparable~~ *[see Drug Interactions (7.1)].*

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בעלון לרופא בוצעו עדכונים נוספים שאינם נכללים בהודעה זו.
העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.
VAQTA מופצת ע"י חברת נובולוג בע"מ.

בברכה,

מיכל סרפר
רוקחת ממונה
MSD ישראל

References:
VAQTA 25U/0.5 M, 50U/ML_SPC_112021