EUVICHOL-S (INACTIVATED ORAL CHOLERA VACCINE)

The vaccine is a liquid formulation of Oral Cholera Vaccine containing O1 of *Vibrio cholerae* inactivated by formalin. The vaccine was developed by EuBiologics Co., Ltd. with the support of International Vaccine Institute (IVI). The vaccine fulfills WHO requirements for cholera.

[COMPOSITION]

One dose (1.5 mL) contains:

Active ingredients:	*V. cholerae* O1 Inaba Phil 6973 El Tor biotype, Formalin inactivated	900 L.E.U.*
	V. cholerae O1 Ogawa Cairo 50 classical biotype, Formalin inactivated	600 L.E.U.*
Excipients:	Sodium phosphate dibasic dihydrate	4.68 mg
	Sodium phosphate monobasic dihydrate	0.97 mg
	Sodium chloride	12.75 mg
	Water for injection	q.s to 1.5 mL

*L.E.U.: Lipopolysaccharide ELISA Unit

[INDICATION]

Prevention of Cholera caused by *Vibrio cholerae* serogroup O1.

[INSTRUCTIONS FOR USE]

1. The vaccine should be administered to anyone above the age of 1 year.
2. Two doses of vaccine should be given at an interval of two weeks.
3. The vaccine is presented as a suspension. Therefore, after shaking the vaccine container rigorously, 1.5 mL of the vaccine should be squirted into the mouth. Take a sip of water if necessary.
4. The frozen vaccines should not be taken.
5. The vaccine is only recommended for oral administration.

[CONTRA-INDICATIONS]

1. The vaccine should not be administered to persons with either known hypersensitivity to any component of the vaccine, or having shown signs of severe reaction due to the previously taken dose.
2. Immunization with Euvichol-S should be delayed in the presence of any acute illness, including acute gastrointestinal illness or acute febrile illness.

[ADVERSE EVENT]

1. Safety was evaluated in 2,529 healthy children, adolescents, and adults (1 year and up to 40 years) were participated in the Phase 3 clinical trial, and all safety information that could not be excluded as drug-related or not drug-related was recorded among the 1,595 people who were administered Euvichol-S.
   Regardless the number of vaccinations received, 151 subjects (<10%) among 1,595 subjects were reported with adverse events. A total of 247 adverse events occurred regardless the number of vaccinations received, based on System Organ Class (SOC), with the highest number of gastrointestinal disorders reported at 29% (71 of 247), followed by general disorders and administration site conditions at 27% (67 of 247), and infections and infestations at 17% (43 of 247). The frequency of each adverse event in children, adolescents, and adults is shown below, followed by the frequency of adverse events in the total population per age group, including both solicited and unsolicited adverse events.

System Organ Class	Adverse Event	Total (n=1,595)	1~5years (n=245)	6~17years (n=360)	18~40years (n=990)
	Total (n=151)	9.5%	20.8%	8.6%	7.0%
Gastrointestinal disorders	Diarrhoea	1.7%	3.3%	0.8%	1.6%
	Vomiting	1.7%	2.9%	2.5%	1.1%
	Nausea	0.5%	1.2%	0.0%	0.5%
	Abdominal pain	0.4%	1.2%	0.3%	0.2%
	Abdominal pain upper	0.1%	0.4%	0.3%	0.0%
	Mouse ulceration	0.1%	0.4%	0.0%	0.0%
General disorders and administration site conditions	Pyrexia	3.6%	11.4%	2.5%	2.0%
	Fatigue	0.6%	0.4%	0.3%	0.7%
	Peripheral swelling	0.1%	0.4%	0.0%	0.0%
Musculoskeletal and connective tissue disorders	Myalgia	0.4%	0.0%	0.3%	0.6%
	Groin pain	0.1%	0.0%	0.3%	0.0%
	Pain in extremity	0.1%	0.4%	0.0%	0.0%
Nervous system disorders	Headache	1.1%	0.0%	1.4%	1.3%
	Burning sensation	0.1%	0.0%	0.0%	0.1%
Metabolism and nutrition disorders	Decreased appetite	0.6%	2.9%	0.0%	0.2%
Respiratory, thoracic and mediastinal disorders	Cough	1.3%	3.7%	1.7%	0.6%
	Oropharyngeal pain	0.1%	0.0%	0.0%	0.2%
Infections and infestations	Nasopharyngitis	2.2%	8.6%	2.2%	0.6%
	Upper respiratory tract infection	0.2%	0.8%	0.3%	0.0%
	COVID-19	0.1%	0.0%	0.0%	0.2%
	Herpes zoster	0.1%	0.0%	0.3%	0.0%
	Scarlet fever	0.1%	0.0%	0.3%	0.0%
	Urinary tract infection	0.1%	0.0%	0.0%	0.1%
Skin and subcutaneous tissue disorders	Eczema	0.2%	1.2%	0.0%	0.0%
Injury, poisoning and procedural complications	Fracture	0.1%	0.4%	0.0%	0.0%
	Road traffic accident	0.1%	0.4%	0.0%	0.0%
Pregnancy, puerperium and perinatal conditions	Premature delivery	0.1%	0.0%	0.0%	0.1%

2. Safety was evaluated in 2,529 healthy children, adolescents, and adults (1 year and up to 40 years) in a Phase 3 clinical trial. Of the 1,595 patients who received Euvichol-S, adverse drug reactions that could not be excluded causality related to the drug is shown below. Regardless of the number of vaccinations, a total of 120 subjects had adverse drug reactions, less than 10% of the total population of 1,595 people.
The frequency of occurrence can be described as very often (≥1/10); often (≥1/100, <1/10); occasionally (≥1/1000, <1/100); rarely (≥1/10000, <1/1000); and very rarely (<1/10000).

System Organ Class	Frequency of occurrence	
	Occasionally (≥1/1000, <1/100)	Often (≥1/100, <1/10)
Gastrointestinal disorders	Vomiting, Nausea, Abdominal pain, Abdominal pain upper, Mouth ulceration	Diarrhoea
General disorders and administration site conditions	Fatigue	Pyrexia
Musculoskeletal and connective tissue disorders	Myalgia	–
Nervous system disorders	Headache	–
Metabolism and nutrition disorders	Decreased appetite	–
Respiratory, thoracic and mediastinal disorders	Cough	–
Infections and infestations	Herpes Zoster, Nasopharyngitis, Upper respiratory tract infection	–
Skin and subcutaneous tissue disorders	Eczema	–

[WARNINGS AND SPECIAL PRECAUTIONS]

1. As with any vaccine, immunization with Euvichol-S may not protect 100% of susceptible persons.
2. As with all vaccines, appropriate medical treatment should always be readily available in case of a rare event of anaphylactic reactions following the administration of the vaccine. For this reason, it is recommended that the person should remain under medical supervision for at least 30 minutes after vaccination.
3. This vaccine contains residual formaldehyde. Caution should be taken in subjects with known hypersensitivity to formaldehyde.
4. The vaccine should not be administered parenterally (intramuscularly, subcutaneously or intravenously).
5. The safety and immune response of Euvichol-S has not been clinically evaluated in individual with HIV/AIDS.

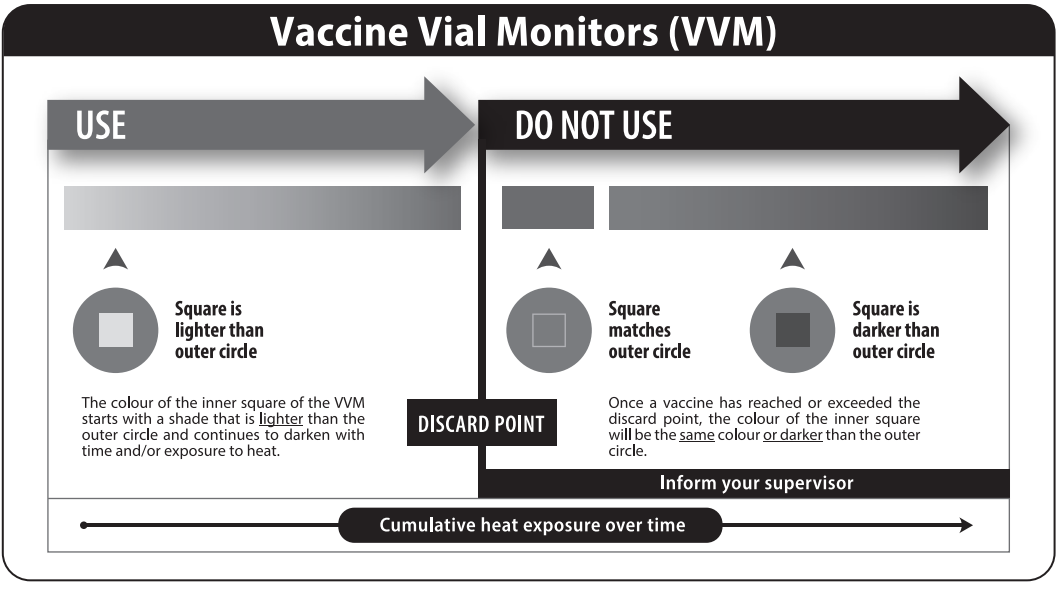
[PREGNANCY AND LACTATION]

No specific clinical studies have been conducted to evaluate the efficacy and safety of Euvichol-S in pregnant or lactating women and for the fetus. Therefore, the vaccine is not recommended for use in pregnancy. Nevertheless, if you are exposed to or will be travelling to an area at risk for cholera, carefully evaluate the benefits and risks of administering this vaccine before considering it.

[STORAGE AND SHELF-LIFE]

The vaccine should be stored at 2℃ ~ 8℃. Do not freeze. The expiry date of the vaccine is 24 months from the date of manufacture.

Vaccine Vial Monitors (VVMs) are a part of the label attached on Euvichol-S supplied through EuBiologics Co., Ltd. The color dot which appears on the label of the vaccine is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vaccine has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its color will change progressively. As long as the color of this square is lighter than the color of the ring, the vaccine can be used. As soon as the color of the central square is the same color as the ring or of a darker color than the ring, the vaccine should be discarded.



[MANUFACTURER]

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