For the use of Registered Medical Practitioner or Hospital or Laboratory only

Killed Bivalent (O1 and O139) Whole Cell Oral Cholera Vaccine

Shanchol™

PRESCRIBING INFORMATION

Qualitative and Quantitative Composition

Each oral dose of 1.5 mL contains

Vaccine Strain	Quantity
V. cholerae O1 Inaba E1 Tor strain Phil 6973 formaldehyde killed	600 Elisa Units (EU) of lipopolysaccharide (LPS)
V.cholerae O1 Ogawa classical strain Cairo 50 heat killed	300 EU of LPS
V.cholerae O1 Ogawa classical strain Cairo 50 formaldehyde killed	300 EU of LPS
V.cholerae O1 Inaba classical strain Cairo 48 heat killed	300 EU of LPS
V.cholerae O139 strain 4260B formaldehyde killed	600 EU of LPS
Thiomersal B.P.	Not more than 0.02% (w/v)
Buffer	q.s to 1.5 mL

THERAPEUTIC INDICATIONS

Shanchol is indicated for active immunization against *Vibrio cholerae.* The vaccine can be administered to anyone above the age of 1 year. Data for the safety and efficacy of the vaccine in infants (less than 1 year of age) is not available. The earliest onset of protection can be expected 7-10 days after the completion of the primary series of vaccine.

POSOLOGY

The recommended dose of the vaccine (1.5 mL) is to be administered orally. The primary immunization schedule consists of two doses given at an interval of two weeks. Shanchol **should not be administered parenterally (intramuscular, subcutaneous or intravenously). The vaccine is only recommended for oral administration.**

CONTRA-INDIACTIONS

Shanchol should not be administered to subjects with either known hypersensitivity to any component of the vaccine, or having shown signs of hypersensitivity after previous administration of the vaccine. Formaldehyde is used during the manufacturing process and trace amount may be present in the final product. Caution should be taken in subjects with known hypersensitivity to formaldehyde. As with all products, the possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. As with other vaccines, immunization with the Shanchol should be delayed in the presence of any acute illness, including acute gastrointestinal illness or acute febrile illness. A minor illness such as mild upper respiratory tract infection is not a reason to postpone immunization.

WARNINGS AND SPECIAL PRECAUTIONS

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and the possible occurrence of undesirable events) and a clinical examination. As with any vaccine, immunization with the Shanchol may not protect 100% of susceptible persons. **This vaccine is also not a substitute for therapy in case of individuals suspected to be suffering from cholera or showing signs and symptoms of an acute episode of gastrointestinal disease.**

Immuno-compromised persons (subsequent to a disease or immunosuppressive therapy) may not obtain the expected immune response after vaccination with the Shanchol If possible, in the opinion of the medical practitioner due consideration should be given to postponing vaccination until after the completion of any immunosuppressive treatment.

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 vaccinee should remain under medical supervision for at least 30 minutes after vaccination.

SPECIAL POPULATIONS

HIV / AIDS

The safety and immune response of Shanchol has not been clinically evaluated in individual with HIV/AIDS.

Pregnancy and Lactation

No specific clinical studies have been performed to evaluate the safety and immunogenicity of Shanchol in pregnant women and for the fetus. **The vaccine is therefore not recommended for use in pregnancy**. However the Shanchol is a killed vaccine that does not replicate, is given orally and acts locally in the intestine. Therefore in the theory, Shanchol should not pose any risk to the human fetus. Administration of Shanchol to pregnant women may be considered after careful evaluation of the benefits and risks in case of a medical emergency or an epidemic.

Pediatric population

Data for the safety and efficacy of the vaccine in infants (less than 1 year of age) is not available. **The vaccine is thus not recommended for use in infants.**

KNOWN ADVERSE REACTIONS ASSOCIATED WITH Shanchol

The following adverse events are known to occur with Shanchol use. Acute Gastroenteritis, Diarrhea, Fever, Vomiting, Abdominal pain, Itching, Rash, Nausea, Weakness, Cough, Vertigo, Dryness of mouth, Oral ulcer (rare), Sore throat (rare) and Yellowing of urine (rare). It has been observed that the incidence of adverse events is less after the second dose as compared to the first.

MECHANISM OF ACTION

Shanchol consists of killed *V.cholerae*. It has been shown to be effective to administer the vaccine orally, which induces local immunity. The vaccine acts locally in the gastrointestinal tract to induce an IgA antibody response (including memory) comparable to that induced by cholera disease itself. The antibacterial intestinal antibodies prevent the bacteria from attaching to the intestinal wall thereby impeding colonization of *V.cholerae* O1 and *V.cholerae O139*. The protection against cholera is specific for both biotype and serotype.

CLINICAL EXPERIENCE

A double-blind, randomized, placebo controlled trial was conducted in Kolkata, India. A total of 101 (50 vaccine and 51 placebo) healthy adults (males and non-pregnant females) aged 18- 40 years and 100 (50 vaccine and 50 placebo) healthy children (males and non-pregnant females) aged 1-17 years were administered two doses of Shanchol or placebo at an interval of two weeks. Following 2 dose immunization, 53% of adult and 80% of children vaccinees showed a ≥4 fold rise in serum *V. cholerae* O1 vibriocidal antibody titers. This study showed that a 2-dose regimen of Shanchol is safe, well-tolerated, and immunogenic in a cholera-endemic area.[1]

A cluster randomized double blind placebo controlled field trial was conducted in Kolkata, India. A total of 66,900 subjects aged one year or older were administered two doses of Shanchol or placebo at an interval of two weeks. The trial subjects were followed up for two years after vaccination. Over two years of follow up there were 20 episodes of cholera in the vaccine group and 68 episodes in the placebo group. Shanchol provided 67% protection against clinically significant *V.cholerae* O1 cholera in an endemic area for at least two years after vaccination. Importantly, protection was seen both in children vaccinated at ages under five years, as well as older persons. There were no statistically significant differences in the occurrence of reported adverse events between recipients of vaccine and placebo. The most common adverse events reported were diarrhoea, fever, vomiting and abdominal pain.[2]

A double blind placebo controlled safety and immunogenicity study was conducted in Dhaka, Bangladesh. A total of 330 adults, toddlers and children (more than one year of age) were administered 2 doses of Shanchol. Overall, the seroconversion (≥ 4 fold rise in serum vibriocidal antibodies) against *V.cholerae* O1 Inaba was observed in 72.53% vaccine recipients as compared to 5.5% in placebo group (p<0.001). Similarly the seroconversion against *V. Cholerae* O1 Ogawa and *V.cholerae* O139 was observed in 74.83% and 46.2% vaccine recepints and 6.7% and 7.2% placebo recipients respectively (p<0.001 for both). In adults, seroconversion (≥ 4fold rise in serum vibriocidal antibodies) against *V.cholerae* O1 Inaba was observed in 60% vaccine receipients as compared to 7.3% in placebo group (p<0.001). Similarly the seroconversion against *V.cholerae* O1 Ogawa and *V. Cholerae* O139 was observed in 72% and 21% vaccine recipients and 9.2% and 5.4% placebo recipients respectively (p<0.001 and 0.017). In children (1-5 years old), seroconversion (≥ 4fold rise in serum vibriocidal antibodies) against *V.cholerae* O1 Inaba was observed in 78.8% vaccine recipients as compared to 4.5% in placebo group (p<0.001). Similarly the seroconversion againt *V.cholerae* O1 Ogawa and *V.cholerae* O139 was observed in 76.25% and 58.8% vaccine recipients and 5.5% and 8.15% placebo recipients respectively (p<0.001 for both). No significant differences were observed in safety events between the vaccine and placebo recipients.[3]

SHELF - LIFE

The expiry date of the vaccine is indicated on the label and packaging.

SPECIAL PRECAUTIONS FOR STORAGE

Shanchol should be stored at +2ºC to +8ºC. **Do not freeze**. Discard if vaccine has been frozen.

PRESERVATION

Glass vials containing 1.5 mL as a single dose.

INSTRUCTION FOR USE/ HANDLING

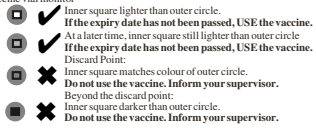
The vaccine is presented as a suspension. After vigorous shaking of the vial, 1.5 mL should be squirted into the mouth of the recipient, followed by water *ad libitum*. The vaccine can alternatively be administered with a disposable syringe (without needle) after removing the contents from the vial and squirted into the mouth of the recipient. Shanchol **should not be administered parenterally (intramuscularly/subcutaneously or intravenously). The vaccine is only recommended for oral administration.**

Do not freeze. Discard if the vaccine has been frozen. Vaccine will be seriously damaged if frozen at temperatures below 0ºC. Exposure to heat will be indicated by the VVM.

VVM are part of the label on all Vaccines supplied through UNICEF. The colour dot that appears on the label of the vial is a VVM. This is a time temperature sensitive dot that provides an indication of the cumulative heat to which the vial 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 colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

The vaccine vial monitor



References:

1.PLoS ONE 2008;3(6):e2323
2.Lancet 2009 ; 374:1694-1702
3.Data on file, Shantha Biotechnics Limited.

Developed, Manufactured and Marketed by:
Shantha Biotechnics Limited
Survey No. 274, Athvelli Village,
Medchal Mandal 501 401
Ranga Reddy District, Andhra Pradesh, INDIA.
Tel:+91-40-23234104,23234105, 23234135,23234136;
Fax +91-40-23234103, 23234133
Email:info@shanthabiotech.co.in
Web: www.shanthabiotech.com

SHANTHA
Part of the sanofi-aventis Group

SBL/SC-Eng/EXP/LT-1.1/U 09 .2011