▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – VAXCHORA® (*Vibrio cholerae*)

1 NAME OF THE MEDICINE

Vibrio cholerae

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of vaccine contains the active ingredient of 4 x 10^8 to 2 x 10^9 of attenuated *Vibrio cholerae* bacteria cells (CVD 103-HgR strain)[1].

[1] Produced by recombinant DNA technology.

This product contains genetically modified organisms (GMOs).

Excipient(s) with known effect: each dose of vaccine contains lactose as sugars, sucrose, and 863 milligrams of sodium.

For the full list of excipients, see section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

VAXCHORA (*Vibrio cholerae*) is provided in a sachet as a powder for suspension (Sachet 2), with an accompanying sachet (Sachet 1) containing effervescent powder (buffer).

The active ingredient is a white to beige powder, and the buffer is a white-to-off-white powder.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

VAXCHORA vaccine is indicated for active immunisation against disease caused by *Vibrio cholerae* serogroup O1 in adults and children aged 2 years and older travelling to cholera-affected countries.

VAXCHORA vaccine should be used in accordance with official recommendations.

The vaccine should not replace standard preventive hygiene measures.

4.2 DOSE AND METHOD OF ADMINISTRATION

Posology

Adults and children aged 2 years and older

A single oral dose should be administered at least 10 days prior to potential exposure to *cholera*.

Revaccination

The safety and effectiveness of revaccination with VAXCHORA vaccine have not been established.

Paediatric population

The safety and efficacy of VAXCHORA vaccine in children less than 2 years have not been established. No data are available.

Method of administration

Oral use.

Preparation for use

To prepare the vaccine for administration, the VAXCHORA active and buffer component sachets are removed from the refrigerator no more than 12 hours at or below 25°C prior to reconstitution.

Eating and drinking should be avoided for 60 minutes before and after oral ingestion of VAXCHORA vaccine.

It is important to mix the sachets in the order described. If the sachets are reconstituted in the incorrect order, the vaccine must be discarded. If the integrity of the sachet has been compromised, or if the vaccine and/or buffer shows signs of yellowing and clumping, then the vaccine/buffer should be discarded.

Step 1: First, the contents of Sachet 1 (a white-to-off-white buffer powder) are added to 100 mL of cold or room temperature (≤25°C) bottled non-carbonated or carbonated drinking water in a cup. Using non-bottled (e.g. tap water) may render the vaccine ineffective. The solution should be stirred until the buffer powder is dissolved.

For children age 2 to 5 years ONLY, half (50 mL) of the buffer solution should then be discarded before proceeding to the next step.

Step 2: The contents of Sachet 2 (containing the active ingredient which is a white-to-beige powder) are then added to the cup and the mixture is stirred for at least 30 seconds. The reconstituted vaccine forms a slightly cloudy suspension that may contain some white particulates. The dose should be drunk within 15 minutes of reconstitution.

If desired, sucrose (no more than 4 grams / 1 teaspoon) or stevia sweetener (no more than 1 gram / ¼ teaspoon) may then be stirred into the suspension. DO NOT add other sweeteners as this may reduce the effectiveness of the vaccine.

The recipient should drink the full contents of the cup at once. Some residue may remain in the cup. The cup should be washed with soap and hot water.

Consumption of less than a half dose may result in decreased protection. If less than half the dose is consumed, consideration may be given to repeating a full dose of VAXCHORA vaccine within 72 hours. The degree of protection added by a repeat dose is unknown.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Allergic reaction to previous ingestion of VAXCHORA vaccine.

Individuals with congenital immune deficiency or receiving immunosuppressive drugs or treatments.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified precautions

Factors affecting protection

VAXCHORA vaccine confers protection specific to *Vibrio cholerae* serogroup O1. Immunisation does not protect against *V. cholerae* O139 or other non-O1 serogroups, which are uncommon causes of disease. VAXCHORA vaccine mimics natural infection, however duration of protection is unknown.

As with any vaccine, immunisation with VAXCHORA vaccine will not provide 100% protection. Vaccinees should adhere to hygiene advice and exercise caution regarding food and water consumed in cholera-affected areas. Rehydration measures are strongly recommended in the event of diarrhea.

The effectiveness of VAXCHORA vaccine has not been established in persons who have pre-existing immunity due to previous exposure to *V. cholerae* or receipt of a cholera vaccine.

The safety and effectiveness of VAXCHORA vaccine have not been established in immunocompromised persons.

Potential risk to contacts

VAXCHORA shedding in the stools was studied for 7 days post-vaccination and was observed in 11.3% of vaccine recipients. The duration of shedding of the vaccine strain is unknown. There is a potential for transmission of the vaccine strain to non-vaccinated close contacts (e.g., household contacts).

Concomitant administration with antibacterial agents and/or chloroquine

Concomitant administration with antibacterial agents and/or chloroquine should be avoided as the protection against cholera may be diminished. Refer to section 4.5.

Gastrointestinal Disease

VAXCHORA vaccine contains live attenuated cholera bacteria that replicate in the gastrointestinal tract of the recipient. In individuals with acute gastroenteritis, vaccination should be postponed until after recovery, because protection against cholera may be diminished. The degree of protection and the effects of vaccination in individuals with chronic gastrointestinal disease are unknown.

Excipients

The vaccine contains lactose as sugars and sucrose. Patients with rare hereditary problems of galactose intolerance, congenital lactase deficiency, glucose-galactose malabsorption, fructose intolerance, or sucrose-isomaltase insufficiency should not take this vaccine.

The vaccine contains 863 mg of sodium per dose, equivalent to 43% of the WHO recommended maximum daily intake of 2 g of sodium for an adult.

Use in the elderly

Safety and effectiveness of VAXCHORA vaccine in adults older than 64 years have not been established. However, this group can be expected to be at risk of more severe complications of disease if infected by cholera.

Paediatric use

VAXCHORA vaccine is approved for use in children from 2 years of age.

Effects on laboratory tests

Interference of VAXCHORA vaccine with laboratory tests has not been studied.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

There should be an interval of 2 hours between the administration of VAXCHORA vaccine and of typhoid vaccine Ty21a (gastro-resistant capsules) as the buffer administered with VAXCHORA vaccine may affect the transit of the capsules through the gastrointestinal tract.

Data from studies with a similar product indicate that the concomitant administration of oral polio vaccine or yellow fever vaccine did not affect the immune response produced by the cholera vaccine.

The effects of concomitant administration of VAXCHORA vaccine with other vaccines has not been studied.

Concomitant administration of VAXCHORA vaccine with systemic antibiotics should be avoided since these agents may prevent a sufficient degree of multiplication to occur in order to induce a protective immune response. VAXCHORA vaccine should not be administered to patients who have received oral or parenteral antibiotics within 14 days prior to vaccination. Oral or parenteral antibiotics should be avoided for 10 days following vaccination with VAXCHORA vaccine.

Data from the study of a previous CVD 103-HgR-based vaccine indicate that immune responses to VAXCHORA vaccine and protection against cholera may be diminished when VAXCHORA vaccine is administered concomitantly with chloroquine. Administer VAXCHORA vaccine at least 10 days before beginning antimalarial prophylaxis with chloroquine.

The vaccine is acid-labile and is administered with a buffer. Eating and drinking should be avoided for 60 minutes before and after taking VAXCHORA vaccine as this may interfere with the protective effect of the buffer.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No human or animal data on the effect of VAXCHORA vaccine on fertility are available.

Use in pregnancy – Pregnancy Category B2

There are limited data from the use of VAXCHORA vaccine in pregnant women.

Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).

VAXCHORA vaccine is not absorbed systemically following oral administration. VAXCHORA vaccine should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the foetus.

Use in lactation.

It is unknown whether VAXCHORA vaccine is excreted in human milk. A risk to the breastfed child cannot be excluded.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The safety of VAXCHORA vaccine was evaluated in four randomised, placebo controlled multicentre clinical trials, with a total of 3235 adults aged 18-64 years of age receiving one dose of VAXCHORA vaccine, and 562 adults receiving a placebo.

Summary of safety profile

Adverse Reactions (Ars) are listed according to the following frequency categories:
Very common ≥ 1/10 (≥ 10%),
Common ≥ 1/100 to < 1/10 (≥ 1% and < 10%),
Uncommon ≥ 1/1000 to < 1/100 (≥ 0.1% and < 1%),
Rare ≥ 1/10,000 to < 1/1000 (≥ 0.01% and < 0.1%) and
Very rare < 1/10,000 (< 0.01%)

The database allowed for the detection of very common, common, uncommon and rare Adverse Events (AEs).

Table 1 below summarises the AEs reported within 28 days after receiving VAXCHORA vaccine with a frequency ≥ 1.0% during clinical studies (referred to as 'Adverse Events').

Table 1: Adverse Events ≥ 1% in Adults: VAXCHORA vaccine vs Placebo Rates Regardless of Relatedness to Vaccine

System Organ Class Preferred Term	VAXCHORA vaccine (N=3235)	Placebo (N=562)
General disorders and administration site conditions		
Fatigue ‡	30.0%	29.5%
Nervous system disorders		
Headache ‡	27.8%	26.0%
Gastrointestinal disorders		
Abdominal pain ‡	18.3%	17.0%
Nausea/Vomiting ‡	17.4%	15.6%

System Organ Class Preferred Term	VAXCHORA vaccine (N=3235)	Placebo (N=562)
Diarrhoea ‡	3.6%	1.6%
Flatulence	1.1%	1.2%
Metabolism and nutrition disorders		
Decreased appetite ‡	15.6%	16.8%
Infections and infestations		
Upper respiratory tract infection	2.1%	2.1%
Musculoskeletal and connective tissue disorders		
Back pain	1.4%	1.1%

‡ Reactogenicity events; N= 3171 for Vaxchora vaccine, N=553 for placebo where N represents number of subjects who completed a memory aid.

The ARs listed in Table 2 were reported during clinical studies in adults within 28 days after receiving VAXCHORA vaccine with a frequency uncommon or rare.

Table 2: Adverse Reactions < 1% in Adults administered VAXCHORA vaccine

Adverse Reactions	Frequency
Blood and lymphatic system disorders	
Lymph node pain	Rare
Ear and labyrinth disorders	
Ear pruritus*, motion sickness*	Rare
Eye disorders	
Eye pain*, eye pruritis*, lacrimation increased*, vision blurred*	Rare
Gastrointestinal disorders	
Flatulence, constipation, abdominal distension, dyspepsia, abnormal faeces, abdominal pain upper, abdominal discomfort, dry mouth, eructation	Uncommon
Gastrointestinal sounds abnormal, faeces discoloured, gastrooesophageal reflux disease, frequent bowel movements*, abdominal tenderness*, anal pruritus*, gastritis*, gastrointestinal pain*, oral pain*, paraethesia oral*, proctitis ulcerative*, rectal haemorrhage*, retching*, stomatitis*, tongue disorder*	Rare
General disorders and administration site conditions	
Pain, pyrexia	Uncommon
chills, irritability, feeling hot, malaise, chest discomfort*, chest pain*, sluggishness*, thirst*	Rare
Infections and infestations	
Upper respiratory tract infection, nasopharyngitis	Rare
Injury, poisoning and procedural complications	
Burn oesophageal*	Rare
Metabolism and nutritional disorders	
Dehydration*, increased appetite*	Rare
Musculoskeletal and connective tissue disorders	
Arthralgia, back pain, neck pain	Uncommon
Muscle spasms, musculoskeletal stiffness, myalgia, pain in extremity*, muscle tightness*	Rare
Nervous system disorders	

Adverse Reactions	Frequency
Dizziness	Uncommon
Dysgeusia, lethargy, presyncope, depressed level of consciousness*, migraine*, paresthesia*, sinus headache*, tremor*	Rare
Psychiatric disorders	
Insomnia	Uncommon
Agitation*, anger*, disorientation*	Rare
Renal and urinary disorders	
Pollakiuria, dysuria*	Rare
Respiratory, thoracic and mediastinal disorders	
Oropharyngeal pain, cough, rhinorrhoea	Uncommon
Nasal congestion*, rhinitis allergic*, sneezing*, throat irritation*	Rare
Skin and subcutaneous tissue disorders	
Rash	Uncommon
Pruritis, angioedema*, cold sweat*, dermatitis*, hyperhidrosis*, night sweats*, rash pruritic*	Rare
Vascular disorders	
Flushing*	Rare

* Occurred in one participant

Paediatric population

A clinical trial was conducted in 550 children aged 2 to 17 years. Based on the results of this trial the type of adverse reactions in children are expected to be similar to those in adults. Some adverse reactions were more common in children than adults, including fatigue (35.7% vs 30.0%), abdominal pain (27.8% vs 18.3%), vomiting (3.8% vs 0.2%), decreased appetite (21.4% vs 15.6%) and pyrexia (2.1% vs 0.7%).

Post-marketing Data

Additional adverse reactions reported during post-marketing surveillance are listed in Table 3.

Table 3: Additional Adverse Reactions from Post-marketing Experience

Adverse Reactions	Frequency
Musculoskeletal and connective tissue disorders	
Mobility decreased*	Rare
Psychiatric disorders	
Anxiety*	Rare

* 2 events each from post-marketing surveillance

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

There have been reports of multiple doses of VAXCHORA vaccine being administered several weeks apart. The adverse reactions reported were comparable to those seen after the recommended dose.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Bacterial vaccines, ATC code: J07AE02.

Mechanism of action

VAXCHORA vaccine contains live attenuated cholera bacteria (*V. cholerae* O1 classical Inaba strain CVD 103-HgR). CVD 103-HgR was constructed from the serogroup O1 classical Inaba strain 569B by deleting the catalytic domain sequence of both copies of the ctxA gene, which prevents the synthesis of the toxic subunit A of cholera toxin, thus preventing synthesis of active cholera toxin (CT). This attenuated strain remains able to synthesize the immunogenic non-toxic B subunit of CT (encoded by the ctxB gene). In addition, a marker was inserted into the hemolysin gene locus (hlyA) to enable differentiation of the vaccine strain from wild type *V. cholerae* O1. CVD 103-HgR elicits a local intestinal and serum antibody response which recognizes native cholera toxin and wild type *V. cholerae*. Due to the inability of CVD 103-HgR to synthesize active cholera toxin subunit A, diarrheal disease normally associated with *V. cholerae* infection is absent.

VAXCHORA vaccine replicates in the gastrointestinal tract of the recipient and induces serum vibriocidal antibody and memory B cell responses. Immune mechanisms conferring protection against cholera following receipt of VAXCHORA vaccine have not been determined, however, rises in serum vibriocidal antibody 10 days after vaccination with VAXCHORA vaccine were associated with protection in a human challenge study.

Clinical trials

Efficacy against cholera challenge

VAXCHORA efficacy against cholera was demonstrated in a human challenge study conducted in 197 healthy adult volunteers mean age 31 years (range 18 to 45, 62.9% male, 37.1% female) in which a subset of VAXCHORA vaccine or placebo recipients were challenged with live *V. cholerae* at 10 days post-vaccination (n=68) or 3 months post-vaccination (n=66). Protective efficacy against moderate to severe diarrhoea is shown in Table 4.

In individuals with blood group O only, the protective efficacy against moderate or severe diarrhoea was 84.8% in the 10-day challenge group (n=19) and 78.4% in the 3-month challenge group (n=20).

Table 4: Diarrheal Volume and Protective Efficacy in the Prevention of Moderate to Severe Diarrhoea Following Challenge with *V. cholerae* O1 El Tor Inaba at 10 Days and 3 Months Post-Vaccination (Intent-to-Treat Population)

Parameter	VAXCHORA vaccine 10 Day Challenge N=35	VAXCHORA vaccine 3 Month Challenge N=33	Combined Placebo 10 Day or 3 Month Challenge N=66
Geometric Mean Diarrheal Volume (mL)	624.2	487.9	3495.1
[95% CI]	[147.2, 2645.9]	[237.3, 1003.5]	[2651.3, 4607.4]
Min, Max	154, 18164	22, 9950	140, 24374
Number of Subjects with Moderate or Severe Diarrhoea (Attack Rate)	2 (5.7%)	4 (12.1%)	39 (59.1%)
Protective Efficacy % [95% CI]	90.3% [62.7%, 100.0%]	79.5% [49.9%, 100.0%]	-

Immunogenicity

The human challenge study showed that vibriocidal seroconversion, defined as a four-fold or greater rise in serum vibriocidal antibody titres from baseline measured 10 days after vaccination, had a nearly one-to-one correlation with protection against moderate-to-severe diarrhoea. Seroconversion was therefore selected as the immunologic bridge between adults age 18 to 45 years in the challenge study and other populations, i.e., older adults and paediatric subjects. Three additional studies evaluated immunogenicity: a large trial in 3146 healthy adults age 18 to 45 years (mean age 29.9, range 18-46, 45.2% male, 54.8% female); a trial in 398 healthy older adults age 46 to 64 years (mean age 53.8, range 46-64, 45.7% male, 54.3% female); and a paediatric trial in healthy subjects age 2-17 years. Prespecified immunobridging analyses, based on differences in seroconversion rates, were determined to demonstrate non-inferiority in seroconversion rate between older adults or paediatric subjects and the adults age 18 to 45 in the large immunogenicity trial.

The seroconversion rates in vaccine and placebo recipients from each trial at 10 days post-vaccination, as well as immunobridging results, are summarised in Table 5 and Table 6. In the challenge study, 79.8% of subjects had seroconverted by 7 days post-vaccination. Seroconversion rates in older adults and paediatric subjects were non-inferior to those in younger adults.

In the three adult studies significant increases in the percentage of anti-O1 lipopolysaccharide (LPS) IgA and IgG memory B cells and anti-cholera toxin IgG memory B cells were seen at 90 and 180 days after vaccination. No relationship between age and memory B cell response was observed. Geometric mean titres (GMTs) of serum vibriocidal antibodies in vaccinated subjects were also significantly higher than the respective GMTs of placebo recipients at 90 and 180 days after immunisation in all age groups. The duration of protection is not known.

Table 5: Vibriocidal Antibody Seroconversion Against Classical Inaba *V. cholerae* Vaccine Strain at 10 Days Post-Vaccination in Adults

Study	VAXCHORA Recipients		Placebo Recipients		Immunobridging: Difference in Seroconversion Rate Compared to Large Trial in 18-45 year olds
(age in years)	N[b]	Seroconversion[a] % [95% CI]	N[b]	Seroconversion[a] % [95% CI[c]]	%[d] [95% CI[c]]
Challenge Trial (18 – 45)	93	90.3% [82.4%, 95.5%]	102	2.0% [0.2%, 6.9%]	-
Large Trial (18 – 45)	2687	93.5% [92.5%, 94.4%]	334	4.2% [2.3%, 6.9%]	-
Older Adults (46 – 64)	291	90.4% [86.4%, 93.5%]	99	0% [0.0%, 3.7%]	−3.1% [−6.7%, 0.4%]

[a] Seroconversion is defined as the percentages of subjects who had at least a 4-fold rise in vibriocidal antibody titer at 10 days post-vaccination compared to baseline.

[b] N=number of subjects with analyzable samples at Day 1 and Day 11.

[c] CI=confidence interval.

[d] Non-inferiority criteria: lower bound of the two-sided 95% confidence interval on the difference in seroconversion rates compared with adults age 18 to 45 years had to be greater than –10 percentage points and the lower bound of the two-sided 95% confidence interval on the proportion of vaccinees who seroconverted 10 days after vaccination had to be equal to or exceed 70%.

Available data on seroconversion rates against other biotypes and serotypes of *V. cholerae* are shown in Table 3. Seroconversion rates for these biotypes and serotypes were not determined in children.

Table 6: Seroconversion Rates 10 Days Post-Vaccination for the Four Major *V. cholerae* O1 Serogroup Biotypes and Serotypes [Immunogenicity Evaluable Population]

Cholera Strain	Younger Adults (18 through 45 year olds) VAXCHORA vaccine		Older Adults (46 through 64 year olds) VAXCHORA vaccine	
	N[a]	%[b] [95% CI[c]]	N[a]	% [95% CI]
Classical Inaba[d]	93	90.3% [82.4%, 95.5%]	291	90.4% [86.4%, 93.5%]
El Tor Inaba	93	91.4% [83.8%, 96.2%]	290	91.0% [87.1%, 94.1%]
Classical Ogawa	93	87.1% [78.5%, 93.2%]	291	73.2% [67.7%, 78.2%]
El Tor Ogawa	93	89.2% [81.1%, 94.7%]	290	71.4% [65.8%, 76.5%]

[a] N=number of subjects with measurements at baseline and 10 days post-vaccination. One subject in the younger adults study did not have a Day 11 measurement and was dropped from the analysis.
[b] Seroconversion is defined as the percentages of subjects who had at least a 4-fold rise in vibriocidal antibody titer at 10 days post-vaccination compared to the titer measured at baseline.
[c] CI=confidence interval.
[d] VAXCHORA vaccine contains the classical Inaba strain of *V. cholerae* O1.

Paediatric population

An immunogenicity trial was conducted in 550 healthy children aged 2 to 17 years (mean age 9.0, range 2-17, 52.0% male, 48.0% female). In the immunogenicity evaluable population (n=466) the ratio of male to female was 52.8% male and 47.2% female. The seroconversion results in vaccine and placebo recipients and immunobridging results are shown in Table 7.

Long-term immunogenicity data are available from a subset of children aged 12 to 17 years. The seroconversion rate ranged from 100% at 28 days post-vaccination to 64.5% at 729 days post-vaccination. The seroconversion results over time are shown in Table 8.

Table 7: Vibriocidal Antibody Seroconversion Against Classical Inaba *V. cholerae* Vaccine Strain at 10 Days Post-Vaccination in Children

Study	VAXCHORA Recipients		Placebo Recipients		Immunobridging: Difference in Seroconversion Rate Compared to Large Trial in 18-45 year olds
(age in years)	N[b]	Seroconversion[a] % [98.3% CI]	N[b]	Seroconversion[a] % [95% CI[c]]	%[d] [96.7% CI]
Paediatric Trial (2 – 17)	399	98.5% [96.2%, 99.4%]	67	1.5% [0.3%, 8.0%]	5.0% [2.8%, 6.4%][c]

[a] Seroconversion is defined as the percentages of subjects who had at least a 4-fold rise in vibriocidal antibody titer at 10 days post-vaccination compared to baseline.

[b] N=number of subjects with analyzable samples at Day 1 and Day 11 in the immunogenicity evaluable population.

[c] CI=confidence interval.

[d] Non-inferiority criteria: lower bound of the two-sided 96.7% confidence interval on the difference in seroconversion rates compared with adults ages 18 to 45 years had to be greater than –10 percentage points and the lower bound of the two-sided 98.3% confidence interval on the proportion of vaccinees who seroconverted 10 days after vaccination had to be equal to or exceed 70%.

Table 8: Vibriocidal Antibody Seroconversion Against Classical Inaba *V. cholerae* Vaccine Strain 10 through 729 Days Post-Vaccination in Children age 12 to 17 Years [Immunogenicity Evaluable Population in the Long-Term Follow-up Sub-study]

Paediatric Trial (12 through 17 year olds) Day Post-Vaccination	**VAXCHORA vaccine** N[b]	**VAXCHORA Seroconversion[a]** % [95% CI[c]]
10	72	100.0% [94.9%, 100.0%]
28	72	100.0% [94.9%, 100.0%]
90	72	88.9% [79.6%, 94.3%]
180	71	83.1% [72.7%, 90.1%]
364	70	68.6% [57.0%, 78.2%]
546	67	73.1% [61.5%, 82.3%]
729	62	64.5% [52.1%, 75.3%]

[a] Seroconversion is defined as the percentages of subjects who had at least a 4-fold rise in vibriocidal antibody titer post-vaccination compared to baseline.

[b] N=number of subjects with analyzable samples at Day 1 and Day 11 in the immunogenicity evaluable population of the long-term follow-up sub-study.

[c] CI=confidence interval.

A subset of patients (N=33) received <80% of the vaccine dose (see Table 9). In this subset, overall seroconversion was 75.8%. Seroconversion was 100% for subjects taking 50-80% of the dose (N=7) and 69.2% for subjects taking <50% of the dose (n=26).

Table 9: Number of Subjects (%) with SVA Seroconversion at 10 Days Post-vaccination Stratified by Portion of Dose Consumed*

	<50% of Dose	≥50 to <80% of Dose	Total (<80% of Dose)
2 to 5 years	11/16 (68.8%)	6/6 (100%)	17/22 (77.3%)
6 to 11 years	6/9 (66.7%)	1/1 (100%)	7/10 (70.0%)
12 to 17 years	1/1 (100%)	0/0	1/1 (100%)
All age groups	18/26 (69.2%)	7/7 (100%)	25/33 (75.8%)

*Among VAXCHORA subjects (modified intent-to-treat population) who consumed less than 80% of expected dose

5.2 PHARMACOKINETIC PROPERTIES

Not applicable.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available

Carcinogenicity
No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Buffer, Sachet 1:

Sodium bicarbonate

Sodium carbonate

Ascorbic acid

Lactose

Active ingredient, Sachet 2:

Sucrose

Hydrolysed casein

Ascorbic acid

Lactose

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

After reconstitution (see section 6.6), the suspension should be consumed within 15 minutes.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in a refrigerator (2°C – 8°C).

VAXCHORA vaccine should be kept refrigerated but may be used if left at or below 25°C up to 12 hours prior to reconstitution.

Avoid exposure to temperatures above 25°C.

Store in the original package.

6.5 NATURE AND CONTENTS OF CONTAINER

Carton box containing one active ingredient sachet (Sachet 2) and one buffer sachet (Sachet 1).

The active ingredient sachet contains 2 g of powder for suspension.

The buffer sachet contains 4.5 g of effervescent powder.

The active ingredient (*Vibrio cholerae* CVD 103-HgR) sachet (Sachet 2) is made from four-ply multilayer foil containing an outer layer of paper, a layer of low-density polyethylene, a layer of aluminium foil and an inner layer of low-density polyethylene.

The buffer sachet (Sachet 1) is made from three-ply multilayer foil containing an outer layer of paper, a middle layer of aluminium foil and an inner layer of low-density polyethylene.

Pack size: 1 box containing 2 sachets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

This medicinal product contains genetically modified organisms. Unused medicinal product must be disposed of in compliance with the local biosafety guidelines.

6.7 PHYSICOCHEMICAL PROPERTIES

Not applicable.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicines (S4)

8 SPONSOR

Australia
Biocelect Pty Ltd
Level 29,
66 Goulburn Street
Sydney
NSW, 2000

Customer enquiries and Medical Information:
Telephone: 1300 848 628
Website: www.biocelect.com/products/
Email: info@biocelect.com

9 DATE OF FIRST APPROVAL

06 September 2023

10 DATE OF REVISION

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
	First issue of the PI