VAXCHORA- cholera vaccine, live, oral
Bavarian Nordic A/S

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VAXCHORA safely and effectively. See full prescribing information for VAXCHORA.

VAXCHORA® (Cholera Vaccine, Live, Oral)
Suspension for Oral Administration

Initial U.S. Approval: 2016

INDICATIONS AND USAGE

VAXCHORA is a vaccine indicated for active immunization against disease caused by *Vibrio cholerae* serogroup O1. VAXCHORA is approved for use in persons 2 through 64 years of age traveling to cholera-affected areas. (1)
Limitations of Use:

- The effectiveness of VAXCHORA has not been established in persons living in cholera-affected areas. (1.1)
- The effectiveness of VAXCHORA has not been established in persons who have pre-existing immunity due to previous exposure to *V. cholerae* or receipt of a cholera vaccine. (1.1)
- VAXCHORA has not been shown to protect against disease caused by *V. cholerae* serogroup O139 or other non-O1 serogroups. (1.1)

DOSAGE AND ADMINISTRATION

- For oral administration only.
- Prepare and administer VAXCHORA in a healthcare setting equipped to dispose of medical waste. (2.3)
- Prepare VAXCHORA by reconstituting the buffer component in 100 milliliters (mL) of **bottled** water (purified, spring, or sparkling [carbonated]); for children 2 through 5 years of age, discard half the reconstituted buffer solution; then add the active component (lyophilized *V. cholerae* CVD 103-HgR). (2.3) After preparation, a single dose of VAXCHORA is 100 mL for persons 6 through 64 years or 50 mL for children 2 through 5 years of age. (3)
- Instruct recipients to avoid eating or drinking for 60 minutes before and after oral ingestion of VAXCHORA. (2.2)
- Administer VAXCHORA a minimum of 10 days before potential exposure to cholera. (2.1)

DOSAGE FORMS AND STRENGTHS

Suspension for oral administration supplied as a packet of the buffer component and a packet of the active component (lyophilized *V. cholerae* CVD 103-HgR). After preparation, a single dose of VAXCHORA is 100 mL for persons 6 years through 64 years of age or 50 mL for children 2 through 5 years of age. (3)

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) to any ingredient of VAXCHORA or to a previous dose of any cholera vaccine. (4)

WARNINGS AND PRECAUTIONS

- The safety and effectiveness of VAXCHORA have not been established in immunocompromised persons. (5.1)
- VAXCHORA may be shed in the stool of recipients for at least 7 days. There is a potential for transmission of the vaccine strain to non-vaccinated close contacts (e.g., household contacts). Use caution when considering whether to administer VAXCHORA to individuals with immunocompromised close contacts. (5.2)

ADVERSE REACTIONS

The most common adverse reactions for adults (incidence > 3%) were tiredness (31%), headache (29%), abdominal pain (19%), nausea/vomiting (18%), lack of appetite (17%) and diarrhea (4%). (6)
The most common adverse reactions for children and adolescents (incidence ≥10%) were:

- Age 12 to <18 years: headache (45%), tiredness (41%), abdominal pain (38%), lack of appetite (29%) and nausea (22%).
- Age 6 to <12 years: tiredness (35%), abdominal pain (27%), headache (26%), lack of appetite (15%) and nausea (14%).
- Age 2 to <6 years: tiredness (31%), loss of appetite (19%), and abdominal pain (17%). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bavarian Nordic A/S at 1-833-365-9596 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

DRUG INTERACTIONS

Avoid concomitant administration of VAXCHORA with systemic antibiotics since these agents may be active against the vaccine strain. Do not administer VAXCHORA to patients who have received oral or parenteral antibiotics within 14 days prior to vaccination. (7.2)
Immune responses to VAXCHORA may be diminished when VAXCHORA is administered concomitantly with chloroquine. Administer VAXCHORA at least 10 days before beginning antimalarial prophylaxis with chloroquine. (7.2)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 2/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VAXCHORA is a vaccine indicated for active immunization against disease caused by *Vibrio cholerae* serogroup O1 in persons 2 through 64 years of age traveling to cholera-affected areas.

1.1 Limitations of Use

The effectiveness of VAXCHORA has not been established in persons living in cholera-affected areas.

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

VAXCHORA has not been shown to protect against disease caused by *V. cholerae* serogroup O139 or other non-O1 serogroups.

2 DOSAGE AND ADMINISTRATION

For oral administration only.

2.1 Dose and Schedule

Administer a single oral dose of VAXCHORA a minimum of 10 days before potential exposure to cholera.

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

2.2 Restrictions on Eating and Drinking

Instruct recipients to avoid eating or drinking for 60 minutes before and after oral ingestion of VAXCHORA.

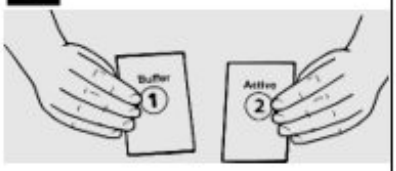
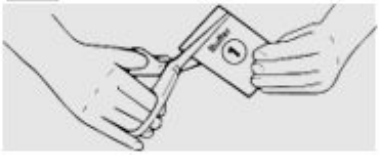
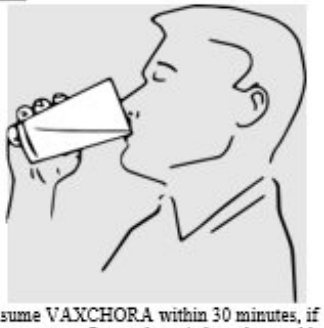
2.3 Preparation, Reconstitution and Administration

Prepare and administer VAXCHORA in a healthcare setting equipped to dispose of

medical waste *[see Disposal Instructions (2.4)]*.

1. Remove the carton from the refrigerator *[see Storage and Handling (16.2)]*. Locate the 2 packets: the buffer component (Packet 1) and the active component (Packet 2).
2. Pour 100 milliliters (mL) of cold or room temperature (41°F-72°F; 5°C-22°C) **bottled** water (purified, spring, or sparkling [carbonated]) into a clean, disposable cup. Do not use tap/faucet water, or any non-purified bottled water, other beverages, or liquids.
3. Use scissors to cut the top off the buffer component packet.
4. Empty buffer component packet contents into cup. Effervescence will occur.
5. Using a disposable stirrer, stir until the buffer component completely dissolves. For children 2 through 5 years of age, discard half of the buffer solution after mixing.
6. Use scissors to cut the top off the active component packet.
7. Empty the active component packet contents (lyophilized *V. cholerae* CVD 103-HgR) into the cup containing the buffer solution.
8. Stir for at least 30 seconds and until active component disperses to form a slightly cloudy suspension that may contain some white particulates.
   If desired, no more than 4 g (1 teaspoon) of sucrose (table sugar) or no more than 1 g (1/4 teaspoon) of non-flavored stevia sweeteners may be added and stirred into the suspension. Do not add any other sweeteners or medicinal flavorings as this can reduce the effectiveness of the vaccine.
9. Consume VAXCHORA within 30 minutes, if sucrose or non-flavored stevia are added. Consume VAXCHORA within 4 hours of reconstitution, if sucrose and non-flavored stevia have not been added, at room temperature around 70 °F (21°C). The recipient should drink the full contents of the cup. Some residue may remain in the cup and should be discarded with the cup.

NOTE: If the packets are reconstituted in the improper order, the vaccine must be discarded *[see Disposal Instructions (2.4)]*.

1  Remove the carton from the refrigerator [see *Storage and Handling (16.2)*]. Locate the 2 packets: the buffer component (Packet 1) and the active component (Packet 2).	2  Pour 100 mL of cold or room temperature (41°F-72°F; 5°C-22°C) **bottled** water (purified, spring, or sparkling [carbonated]) into a clean, disposable cup. Do not use tap/faucet water or any non-purified bottled water, other beverages, or liquids.	3  Use scissors to cut the top off the buffer component packet.
4  Empty buffer component packet contents into cup. Effervescence will occur.	5  Using a disposable stirrer, stir until the buffer component completely dissolves. **For children 2 through 5 years of age, discard half of the mixed buffer solution.**	6  Use scissors to cut the top off the active component packet.
7  Empty the active component packet contents (lyophilized *V. cholerae* CVD 103-HgR) into the cup containing the buffer solution.	8  Stir for at least 30 seconds and until the active component disperses to form a slightly cloudy suspension that may contain some white particulates. If desired no more than 4 g (1 teaspoon) of sucrose (table sugar) or no more than 1 g (1/4 teaspoon) of a non-flavored stevia sweetener may be added and stirred into the suspension.	9  Consume VAXCHORA within 30 minutes, if sucrose or non-flavored stevia have been added. Consume VAXCHORA within 4 hours of reconstitution, if sucrose or non-flavored stevia have not been added, at room temperature around 70°F (21°C). The recipient should drink the full contents of the cup. Some residue may remain in the cup and should be discarded with the cup.

2.4 Disposal Instructions

Dispose of the cup, packets, and stirrer according to standard procedures for medical waste.

Inactivate any spilled vaccine and clean any non-disposable equipment used in the preparation of VAXCHORA with 70% isopropyl alcohol or 10% bleach solution.

3 DOSAGE FORMS AND STRENGTHS

VAXCHORA is a suspension for oral administration. Before reconstitution, each dose of VAXCHORA is supplied as a foil packet of buffer and an accompanying foil packet of the active component (lyophilized *V. cholerae* CVD 103-HgR). After reconstitution, a single dose of VAXCHORA is 100 mL (50 mL for children 2 through 5 years of age).

4 CONTRAINDICATIONS

Do not use in persons who have a history of severe allergic reaction (e.g., anaphylaxis) to any ingredient of VAXCHORA or to a previous dose of any cholera vaccine *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Altered Immunocompetence

The safety and effectiveness of VAXCHORA have not been established in immunocompromised persons *[see Immunocompromised Individuals (8.6)]*.

5.2 Shedding and Transmission

VAXCHORA may be shed in the stool of recipients for at least 7 days. There is a potential for transmission of the vaccine strain to non-vaccinated close contacts (e.g., household contacts) *[see Pharmacodynamics (12.2)]*. Use caution when considering whether to administer VAXCHORA to individuals with immunocompromised close contacts.

6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

The most common adverse reactions for adults (incidence > 3%) were tiredness (31%), headache (29%), abdominal pain (19%), nausea/vomiting (18%), lack of appetite (17%) and diarrhea (4%).

The most common adverse reactions for children and adolescents (incidence ≥10%) were:

- Cohort 1 - age 12 to <18 years: headache (45%), tiredness (41%), abdominal pain (38%), lack of appetite (29%) and nausea (22%).
- Cohort 2 - age 6 to <12 years: tiredness (35%), abdominal pain (27%), headache (26%), lack of appetite (15%) and nausea (14%).
- Cohort 3 - age 2 to <6 years: tiredness (31%), lack of appetite (19%), and abdominal pain (17%).

6.1 Clinical Trials Experience

Trials in Adults

The safety of VAXCHORA was evaluated in four randomized, placebo-controlled, multicenter clinical trials. A total of 3235 adults 18 through 64 years of age received one dose of VAXCHORA and 562 received placebo [physiologic saline (N=551) or lactose (N=11)]. Overall, the mean age was 32.5 years; 53.8% of trial participants were female; 67.1% were White, 27.3% were Black or African American, 1.8% were Asian, 1.7% were multiracial, 1.3% were other, 0.6% were American Indian or Alaskan Native and 0.3% were Native Hawaiian or Pacific Islander. There were 9.3% Hispanic or Latino participants.

Solicited Adverse Reactions

Adults 18 through 45 years of age received VAXCHORA in a multi-center, double-blind, randomized (8:1), placebo-controlled trial conducted in the United States and Australia (Study 1). The safety analysis set included 2789 VAXCHORA recipients. Solicited adverse reactions were recorded daily for 7 days following vaccination. Table 1 presents the frequency and severity of solicited adverse reactions observed within 7 days following receipt of VAXCHORA or placebo in Study 1.

Table 1: Rates of Solicited Adverse Reactions Reported in VAXCHORA Trial Participants 18 to 45 Years of Age During 7 Days Post-Vaccination − Study 1[a]

Adverse Reaction	VAXCHORA (N=2789)[b] %	Placebo (Saline) (N=350)[b] %
Tiredness	31.3	27.4
Mild	18.7	16.3
Moderate	12.0	9.9
Severe	0.7	1.2
Potentially life-threatening	0.0	0.0
Headache	28.9	23.6
Mild	18.9	14.6
Moderate	9.6	8.8
Severe	0.5	0.3
Potentially life-threatening	0.0	0.0
Abdominal Pain	18.7	16.9
Mild	12.1	12.0
Moderate	6.2	5.0
Severe	0.4	0.0
Potentially life-threatening	0.0	0.0
Nausea/Vomiting	18.3	15.2
Mild	13.3	11.4
Moderate	4.7	3.8
Severe	0.3	0.0
Potentially life-threatening	0.0	0.0
Lack of Appetite	16.5	16.6
Mild	11.7	12.2
Moderate	4.4	4.4

Severe	0.3	0.0
Potentially life-threatening	0.0	0.0
Diarrhea	3.9	1.2
Mild	2.4	0.9
Moderate	0.7	0.3
Severe	0.8	0.0
Potentially life-threatening	0.04	0.0
Fever	0.6	1.2
Mild	0.2	0.3
Moderate	0.3	0.9
Severe	0.07	0.0
Potentially life-threatening	0.04	0.0

[a] Data are derived from Study 1 (NCT02094586).
[b] N represents number of subjects who completed a memory aid.
Grading scales are defined as follows:
Tiredness, Headache, Abdominal Pain, Nausea, Lack of Appetite: Mild = no interference with activity, Moderate = Some interference with activity, Severe = significant, prevents daily activity, Potentially Life Threatening = emergency room (ER) visit or hospitalization.
Vomiting: Mild = 1-2 episodes/24 hours, Moderate = >2 episodes/24 hours, Severe = requires intravenous hydration, Potentially Life Threatening = ER visit or hospitalization for hypotensive shock.
Diarrhea: Mild = 4 loose stools/24 hours, Moderate = 5 loose stools/24 hours, Severe = ≥6 loose stools /24 hours, Potentially Life Threatening = ER visit or hospitalization.
Fever: Mild = 38.0-38.4ºC/100.4-101.1ºF, Moderate = 38.5-38.9ºC/101.2-102.0ºF, Severe = 39.0-40.0ºC/102.1-104.0ºF, Potentially Life Threatening = >40.0 ºC/104.0 ºF.

Serious Adverse Events

In a pooled analysis of the four clinical studies, 0.6% (20/3235) of VAXCHORA recipients and 0.5% (3/562) of placebo recipients reported a serious adverse event within 6 months post-vaccination. None of these events were considered to be related to vaccination.

Pediatric Trial

The safety of VAXCHORA in children was evaluated in one randomized, placebo-controlled, multicenter clinical trial. A total of 468 children 2 through 17 years of age received one dose of VAXCHORA and 75 received placebo (physiologic saline). The mean age was 9.0 years; 51.6% were male; 59.5% were White, 31.3% were Black, 7.7% were multiracial, 0.9% were Asian, and 0.6% were American Indian/Alaskan Native. There were 8.7% Hispanic or Latino participants.

Solicited Adverse Reactions

Children 2 through 17 years of age received VAXCHORA in a multi-center, double-blind, randomized (6:1), placebo-controlled trial conducted in the United States (Study 5). Randomization was stratified by age, and children were enrolled in three separate age cohorts: 12 to < 18 years (Cohort 1), 6 to < 12 years (Cohort 2), and 2 to < 6 years (Cohort 3). The safety analysis set included 468 VAXCHORA recipients and 75 placebo recipients. Solicited adverse reactions were recorded daily for 7 days following vaccination. Table 2 presents the frequency and severity of solicited adverse reactions

observed within 7 days following receipt of VAXCHORA or placebo in Study 5 for the 3 study cohorts.

Table 2: Rates of Solicited Adverse Reactions Reported in VAXCHORA Pediatric Trial (Study 5) Participants 2 to 17 Years of Age During 7 Days Post-Vaccination by Age cohort

Adverse Reaction	Cohort 1 Ages 12 to <18 years VAXCHORA (N=165)[b] %	Cohort 1 Ages 12 to <18 years Placebo (Saline) (N=24)[b] %	Cohort 2 Ages 6 to <12 years VAXCHORA (N=157)[b] %	Cohort 2 Ages 6 to <12 years Placebo (Saline) (N=25)[b] %	Cohort 3 Ages 2 to <6 years VAXCHORA (N=146)[b] %	Cohort 3 Ages 2 to <6 years Placebo (Saline) (N=26)[b] %
Tiredness	40.6	37.5	35.0	32.0	30.8	23.1
Mild	31.5	33.3	22.3	20.0	19.2	15.4
Moderate	8.5	0.0	12.1	12.0	11.6	7.7
Severe	0.6 [c]	4.2	0.6	0.0	0.0	0
Headache	44.8	45.8	26.1	24.0	8.9	7.7
Mild	34.5	45.8	19.1	20.0	6.8	3.8
Moderate	9.7	0.0	5.7	4.0	2.1	3.8
Severe	0.6	0.0	1.3	0.0	0.0	0.0
Abdominal Pain	37.6	16.7	27.4	24.0	17.1	15.4
Mild	28.5	12.5	23.6	16.0	14.4	15.4
Moderate	8.5	4.2	3.8	8.0	2.7	0.0
Severe	0.6	0.0	0.0	0.0	0.0	0.0
Lack of Appetite	29.1	12.5	15.3	20.0	19.2	11.5
Mild	23.6	12.5	12.7	16.0	12.3	7.7
Moderate	5.5	0.0	1.9	4.0	6.8	3.8
Severe	0.0	0.0	0.6	0.0	0.0	0.0
Nausea	22.4	25.0	14.0	16.0	6.8	15.4
Mild	17.0	20.8	12.1	8.0	6.2	15.4
Moderate	4.8	4.2	1.9	8.0	0.7	0.0
Severe	0.6	0.0	0.0	0.0	0.0	0.0
Vomiting	5.5	0.0	4.5	0.0	1.4	11.5
Mild	3.6	0.0	2.5	0.0	1.4	7.7
Moderate	1.2	0.0	1.9	0.0	0.0	3.8
Severe	0.6	0.0	0.0	0.0	0.0	0.0
Fever	1.2	0.0	3.2	4.0	2.1	3.8
Mild	0.6	0.0	0.0	0.0	0.7	0.0
Moderate	0.0	0.0	0.6	4.0	0.7	0.0
Severe	0.6	0.0	2.5	0.0	0.7 [d]	3.8
Diarrhea	3.6	4.2	0.0	0.0	0.7	0.0

Mild	1.8	0.0	0.0	0.0	0.7	0.0
Moderate	0.0	4.2	0.0	0.0	0.0	0.0
Severe	1.8	0.0	0.0	0.0	0.0	0.0

[a] Data are derived from Study 5 (NCT03220737).
[b] N represents number of subjects with a completed a memory aid.
[c] Includes 1 case evaluated in the emergency room for an associated viral pharyngitis considered not related to vaccination.
[d] Includes 1 case with temperature greater than 40°C considered not related to vaccination
Pediatric Grading scales are defined as follows:
Tiredness, Headache, Abdominal Pain, Nausea, Lack of Appetite: Mild = no interference with activity, Moderate = Some interference with activity, Severe = significant, prevents daily activity, Potentially Life Threatening = emergency room (ER) visit or hospitalization.
Vomiting: Mild = 1-2 episodes/24 hours, Moderate = >2 episodes/24 hours, Severe = requires intravenous hydration, Potentially Life Threatening = ER visit or hospitalization for hypotensive shock.
Diarrhea: Mild = 4 loose stools/24 hours, Moderate = 5 loose stools/24 hours, Severe = ≥6 loose stools /24 hours, Potentially Life Threatening = ER visit or hospitalization.
Fever: Mild = 38.0-38.4ºC/100.4-101.1ºF, Moderate = 38.5-38.9ºC/101.2-102.0ºF, Severe = 39.0-40.0ºC/102.1-104.0ºF, Potentially Life Threatening = >40.0 ºC/104.0 ºF.

In total, 13.2% of VAXCHORA recipients reported an unsolicited adverse event that was considered related to study treatment, compared to 9.3% for placebo recipients.

The most frequent unsolicited adverse event for VAXCHORA was loose stool in Cohort 1 (13.9%), Cohort 2 (11.5%) and Cohort 3 (5.5%).

Serious Adverse Events

In Study 5, 0.2% (1/468) of VAXCHORA recipients and 1.3% (1/75) of placebo recipients reported a serious adverse event within 6 months post-vaccination. None of these events were considered to be related to vaccination.

7 DRUG INTERACTIONS

7.1 Food and Drink

Avoid food or drink for 60 minutes before and after vaccine administration *[see Restrictions on Eating and Drinking (2.2)]*.

7.2 Concomitant Vaccines or Medications

Vaccines

No data are available on concomitant administration of VAXCHORA with other vaccines.

Antibiotics

Avoid concomitant administration of VAXCHORA with systemic antibiotics since these agents may be active against the vaccine strain and prevent a sufficient degree of multiplication to occur in order to induce a protective immune response. Do not administer VAXCHORA to patients who have received oral or parenteral antibiotics within

14 days prior to vaccination.

Antimalarial Prophylaxis

Data from a study with a similar product indicate that the immune responses to VAXCHORA may be diminished when VAXCHORA is administered concomitantly with chloroquine. Administer VAXCHORA at least 10 days before beginning antimalarial prophylaxis with chloroquine.

7.3 Immunosuppressive Treatments

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to VAXCHORA *[see Use in Specific Populations (8.6)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

VAXCHORA is not absorbed systemically following oral administration, and maternal use is not expected to result in fetal exposure to the drug.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Maternal cholera disease is associated with adverse pregnancy outcomes including fetal death.

Fetal/neonatal adverse reactions

The vaccine strain may be shed in the stool of the vaccinated mother for at least 7 days, with a potential for transmission of the vaccine strain from mother to infant during vaginal delivery.

8.2 Lactation

Risk Summary

VAXCHORA is not absorbed systemically by the mother following oral administration, and breastfeeding is not expected to result in exposure of the child to VAXCHORA.

8.4 Pediatric Use

The safety and effectiveness of VAXCHORA have not been established in children younger than 2 years of age.

8.5 Geriatric Use

The safety and effectiveness of VAXCHORA have not been established in adults 65 years of age or older.

8.6 Immunocompromised Individuals

The safety and effectiveness of VAXCHORA have not been established in immunocompromised individuals. The immunologic response to VAXCHORA may be diminished in immunocompromised individuals *[see Drug Interactions (7.3)]*.

11 DESCRIPTION

VAXCHORA (Cholera Vaccine, Live, Oral) is a live, attenuated bacterial vaccine suspension for oral administration containing the *V. cholerae* 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 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.

The vaccine strain is grown in fermentors under controlled conditions in medium containing casamino acids, yeast extract, mineral salts, and an anti-foaming agent. The bacteria are concentrated by ultrafiltration before addition of a stabilization solution containing ascorbic acid (an antioxidant), Hy-Case SF (hydrolyzed casein [a protein derived from cow's milk], a cryoprotectant), and sucrose (a cryoprotectant). The stabilized bacteria are lyophilized, milled, and blended with anhydrous lactose (a bulking agent). The active component blend is filled into packets.

The buffer component is manufactured by blending together sodium bicarbonate (a gastric acid neutralizer), sodium carbonate (a buffer), ascorbic acid (a buffer and water chlorine neutralizer), and anhydrous lactose (a manufacturing flow aid). The buffer component blend is filled into packets. One buffer component packet and one active component packet are packaged into individual single dose cartons for distribution.

After reconstitution, VAXCHORA contains 4×10^8 to 2×10^9 colony forming units (CFU) of live attenuated *V. cholerae* CVD 103-HgR. The resulting suspension should be slightly cloudy and may contain white particulates. The active and buffer ingredients are shown in Table 3.

Table 3: Vaccine Composition

Active Component Packet Ingredient	**Active Component Packet Quantity/packet**
V. cholerae CVD 103-HgR	4×10^8 to 2×10^9 CFU[a]
Sucrose	≤ 165.37 mg[b]
Hy-Case SF (hydrolyzed casein)	≤ 17.11 mg
Ascorbic acid	≤ 8.55 mg
Anhydrous lactose	≤ 2.09 g[c]
Buffer Component Packet Ingredient	**Buffer Component Packet Quantity/packet**
Sodium bicarbonate	2.16–2.41 g
Sodium carbonate	0.24-0.49 g
Ascorbic acid	1.50–1.80 g

Anhydrous lactose	0.18–0.22 g

[a] CFU=colony forming units.
[b] mg=milligrams.
[c] g=grams.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

VAXCHORA contains live attenuated cholera bacteria that replicate in the gastrointestinal tract of the recipient. Immune mechanisms conferring protection against cholera following receipt of VAXCHORA have not been determined. However, rises in serum vibriocidal antibody 10 days after vaccination with VAXCHORA were associated with protection in a human challenge study (Study 2) *[see Immunogenicity (14.2)]*.

12.2 Pharmacodynamics

Shedding of the vaccine strain was evaluated in the first 7 days post-vaccination in a study of 53 healthy adult vaccine recipients (Study 3). VAXCHORA was shed in the stools of 11.3% [95% CI 4.3%, 23.0%] of vaccine recipients on any day through 7 days post-vaccination. During the 7 days post-vaccination, the proportion of subjects shedding was highest on day 7 (7.5% [95% CI 2.1%, 18.2%]). The duration of shedding of the vaccine strain is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

VAXCHORA has not been evaluated for the potential to cause carcinogenicity or genotoxicity, or to impair fertility.

14 CLINICAL STUDIES

14.1 Efficacy Against *V. cholerae* Challenge

Study 2 was a randomized, double-blind, saline placebo-controlled *V. cholerae* challenge study conducted in the US. Subjects 18 through 45 years of age (N=197) with no prior history of cholera infection or travel to a cholera-endemic area in the previous 5 years were randomized according to a 1:1 ratio to receive one dose of VAXCHORA or placebo. In order to identify the subset of subjects to be challenged, an unblinded statistician prepared four randomly ordered lists of subjects per site, one list each for vaccine recipients with blood type O, vaccine recipients with non-O blood types, placebo recipients with blood type O, and placebo recipients with non-O blood types. This was done to maintain a minimum of 60% blood group O subjects in each treatment group. Individuals with type O blood are less likely to be infected with *V. cholerae*, but are at risk for developing severe cholera if infected. Each site was provided with a blinded version of the four lists specific to its site and advised on the number of subjects from each list to challenge. In the event that a subject was determined to be ineligible for challenge, the site was instructed to select the next subject from the same list as the ineligible subject.

The challenges were split into 2 cohorts for 10 day and 3 month challenges. Subjects were admitted to an inpatient unit. Subjects had nothing by mouth from midnight before ingestion of the challenge strain, except for water, and had nothing by mouth for 90 minutes after ingestion of the challenge strain. Approximately 1 minute prior to challenge, subjects ingested 120 mL sodium bicarbonate ($NaHCO_3$) buffer. The oral challenge consisted of 1 x 10^5 CFU live wild type *V. cholerae* El Tor Inaba N16961 in 30 mL $NaHCO_3$ buffer at 10 days or 3 months post-vaccination. The co-primary objectives were to demonstrate the efficacy of a single dose of VAXCHORA in the prevention of moderate to severe diarrhea following challenge at 10 days and 3 months post-vaccination. Moderate to severe diarrhea was defined as cumulative diarrheal purge ≥ 3 liters (L) within 10 days after challenge. Diarrheal stool was defined as ≥ 2 unformed stools (takes shape of container) collected during a 48 hour period ≥ 200 grams (g) or a single unformed stool ≥ 300 g. Subjects were instructed to collect every stool from the time of challenge until discharge from the inpatient unit. Nursing staff or study personnel inspected all stool, graded the consistency of the stool and calculated the total weight of diarrheal stool per day. Weight of stool was converted to volume using the formula 1 g=1 mL. VAXCHORA recipients challenged at 10 days post-vaccination and VAXCHORA recipients challenged at 3 months post-vaccination were compared with a pooled group of placebo (saline) recipients challenged at 10 days or 3 months post-vaccination.

Of the 95 VAXCHORA recipients, 68 were challenged; 35 were challenged at 10 days post-vaccination and 33 were challenged at 3 months post-vaccination. Of the 102 placebo recipients, 66 were challenged; 33 were challenged at 10 days post-vaccination and 33 at 3 months post-vaccination. Among all randomized subjects, the mean age was 31.0 years. Overall, the mean age of the challenge population was 31.4 years. More males were in the vaccine group (71.6%) compared to the placebo group (54.9%). The majority of randomized subjects were Black (67.5%), 29.4% were White, 0.5% were American Indian/Alaskan Native, 0.5% were Asian, and 2.0% were other. There were 4.6% Hispanic or Latino participants. Overall 50.3% had blood type O. Among subjects selected for either challenge cohort, more males were challenged in the vaccine group (76.5%) compared to the placebo group (57.6%). The majority (70.9%) of the challenge population were Black, 25.4% were White, 0.7% were American Indian/Alaskan Native, 0.7% were Asian, and 2.2% were other. There were 3.7% Hispanic or Latino participants. Overall, 56.0% of challenged subjects had blood type O.

Vaccine efficacy against the occurrence of moderate to severe diarrhea at 10 days post-vaccination was 90.3% [95% CI 62.7%, 100.0%] and at 3 months post-vaccination was 79.5% [95% CI 49.9%, 100.0%] (Table 4).

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

Parameter	VAXCHORA 10 Day Challenge[a,c] N=35[d]	VAXCHORA 3 Month Challenge[a,c] N=33[d]	Combined Placebo[a,b] 10 Day or 3 Month Challenge[c] N=66[d]
Number of Subjects with Moderate or	2 (5.7%)	4 (12.1%)	39 (59.1%)

Severe Diarrhea (Attack Rate)[e]		
Vaccine Efficacy %[f,g]	90.3%	79.5%
[95% CI[h]]	[62.7%, 100.0%]	[49.9%, 100.0%]

[a] Data are derived from Study 2 (NCT01895855).
[b] Combined placebo group comprised of all placebo recipients who were challenged at either 10 days (N=33) or 3 months (N=33) following vaccination.
[c] Challenge strain was *V. cholerae* O1 El Tor Inaba N16961.
[d] N=number of subjects challenged in each group.
[e] Moderate or severe diarrhea (≥ 3 liters of diarrhea) within 10 days after challenge.
[f] Vaccine Efficacy=[(Attack Rate in Placebo Group - Attack Rate in Vaccine Group)/Attack Rate in Placebo Group] x 100.
[g] Pre-specified criteria for success were that the lower bound of the two-sided 95% confidence interval for vaccine efficacy must be ≥30% in both the 10 Day and 3 Month challenge groups.
[h] CI=confidence interval.

14.2 Immunogenicity

Vibriocidal Antibody Against the Vaccine Strain (classical Inaba)

A vibriocidal antibody assay was used to measure serum levels of neutralizing antibodies against the vaccine strain.

Study 2 was a randomized, double-blind, saline placebo-controlled *V. cholerae* challenge study conducted in adults 18 through 45 years of age. In the subset of subjects challenged in Study 2, 91% [95% CI 82%, 97%] of vaccinees seroconverted prior to challenge and 9% developed moderate to severe cholera following challenge, while 2% of placebo recipients seroconverted prior to challenge and 59% developed moderate to severe cholera following challenge. Seroconversion was defined as a ≥ 4-fold rise in serum vibriocidal antibody from baseline to 10 days post vaccination. Based on the observed association between seroconversion and protection from *V. cholerae* disease, seroconversion rate at 10 days post-vaccination was used to evaluate response to vaccination in other age groups.

Study 1 was a randomized, double-blind, saline placebo-controlled safety and immunogenicity study conducted in the US and Australia. A total of 3146 subjects 18 through 45 years of age not previously exposed to cholera were randomized 8:1 to receive one dose of VAXCHORA or placebo. The mean age was 29.9 years; 45.2% were male; 68.3% were White, 25.6% were Black, 2.0% were Asian, 1.9% were multiracial, 1.4% were other, 0.4% were American Indian/Alaskan Native, and 0.3% were Native Hawaiian/Pacific Islander. There were 10.0% Hispanic or Latino participants.

In this study, classical Inaba vibriocidal antibody seroconversion rates were 93.5% [95% CI 92.5%, 94.4%] in vaccine recipients and 4% [95% CI 2%, 7%] in placebo recipients at 10 days post-vaccination.

Study 4 was a randomized, double-blind, placebo-controlled safety and immunogenicity study conducted in the US. A total of 398 subjects 46 through 64 years of age with no prior history of cholera infection or travel to a cholera-endemic area in the previous 5 years were randomized 3:1 to receive one dose of VAXCHORA or placebo. Overall, the mean age of the randomized population was 53.8 years; 45.7% were male; 74.9% were

White, 21.9% were Black, 1.8% were American Indian/Alaskan Native, 0.5% were Asian, 0.5% were multiracial, 0.3% were Native Hawaiian/Pacific Islander, and 0.3% were other. There were 7.5% Hispanic or Latino participants.

Vibriocidal antibody seroconversion rates at 10 days post-vaccination for the classical Inaba strain among 46 through 64-year-old subjects in Study 4 were compared to those in 18 through 45-year-old subjects in Study 1. VAXCHORA recipients from Study 1 were in the same age group as those in Study 2, the *V. cholerae* challenge study.

Adults 46 through 64 years were shown to have a non-inferior rate of classical Inaba vibriocidal antibody seroconversion at 10 days post-vaccination compared to adults 18 through 45 years of age (Table 5).

Table 5: Vibriocidal Antibody Seroconversion Against Classical Inaba V. cholerae Vaccine Strain at 10 Days Post-Vaccination in Adults 46 through 64 Years of Age (Study 4) Compared to Adults 18 through 45 Years of Age (Study 1) [Bridging Analysis Population]

Study [a]	Dose/CFU	VAXCHORA N[b]	VAXCHORA Seroconversion % [95% CI[c]]
Study 4 (46 through 64-year-olds)	1×10^9	291	90.4% [86.4%, 93.5%]
Study 1 (18 through 45-year-olds)	1×10^9	2687	93.5% [92.5%, 94.4%]
Difference in Seroconversion Rates[d,e]			−3.1% [−6.7%, 0.4%]

[a] Data are derived from Study 1 (NCT02094586) and Study 4 (NCT02100631).
[b] N=number of subjects with analyzable samples at Day 1 and Day 11.
[c] CI=confidence interval.
[d] 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.
[e] Pre-specified success criterion was that the lower bound of the two-sided 95% confidence interval on the difference in seroconversion rate (Study 4 minus Study 1) must be greater than -10 percentage points.

Vibriocidal Antibody Against Classical Ogawa, El Tor Inaba and El Tor Ogawa

V. cholerae serogroup O1 consists of four major subtypes: classical Inaba, classical Ogawa, El Tor Inaba and El Tor Ogawa. Serum vibriocidal antibody against the three types of *V. cholerae* not contained in the vaccine, namely classical Ogawa, El Tor Inaba and El Tor Ogawa, was also measured in Study 2 and Study 4. The percentages of vaccine recipients who seroconverted against each of the 4 major biotype/serotypes of *V. cholerae* serogroup O1 at 10 days post-vaccination (71.4% to 91.4%) are shown in Table 6.

Table 6: Seroconversion Rates 10 Days Post-Vaccination for the Four Major V. cholerae O1 Serogroup Biotypes and Serotypes in Studies 2 and 4

[Immunogenicity Evaluable Population]

Cholera Strain	Study 2[a] (18 through 45-year-olds) VAXCHORA N[b]	Study 2[a] (18 through 45-year-olds) VAXCHORA %[c] [95% CI[d]]	Study 4[a] (46 through 64-year-olds) VAXCHORA N[b]	Study 4[a] (46 through 64-year-olds) VAXCHORA % [95% CI]
Classical Inaba[e]	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] Data are derived from Study 2 (NCT01895855) and Study 4 (NCT02100631).
[b] N=number of subjects with measurements at baseline and 10 days post-vaccination. One subject in Study 2 did not have a Day 11 measurement and was dropped from the analysis.
[c] 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.
[d] CI=confidence interval.
[e] VAXCHORA contains the classical Inaba strain of *V. cholerae* O1.

Pediatric Trial - Vibriocidal Antibody Against the Vaccine Strain (classical Inaba)

The effectiveness of VAXCHORA for the pediatric population 2 through 17 years of age was demonstrated following comparison of the immune response to *V. cholerae* in children and adolescents to the immune response in adults following Vaxchora (immunobridging).

Study 5 was a randomized, double-blind, saline placebo-controlled safety and immunogenicity study conducted in the US. A total of 550 subjects 2 through 17 years of age not previously exposed to cholera were randomized 6:1 to receive one dose of VAXCHORA (1×10^9 CFU/dose) or placebo. Randomization was stratified by age into 3 age cohorts:

- Cohort 1: 12 to <18 years of age
- Cohort 2: 6 to <12 years of age
- Cohort 3: 2 to <6 years of age

In this study, classical Inaba vibriocidal antibody seroconversion rates at 10-days post-vaccination in children 2 through 17 years of age were compared to seroconversion rates in adults 18 through 45 years of age.

Immunobridging results for VAXCHORA, at 10 days post-vaccination, are shown in Table 7. The rate of seroconversion among pediatric placebo recipients was 1.5% [95% CI 0.3%, 8.0%] at 10 days post-vaccination.

Table 7: Vibriocidal Antibody Seroconversion Against Classical Inaba V. cholerae Vaccine Strain at 10 Days Post-Vaccination in Children aged 2 through 17 Years (Study 5) Compared to Adults 18 through 45 Years of Age (Study 1) [Bridging Analysis Population[b]]

Study [a]	Dose/CFU	VAXCHORA N[b]	VAXCHORA Seroconversion % [98.3% CI[c]]
Study 5 (2 through 17-year-olds)	1×10^9	399	98.5% [96.2%, 99.4%]
Study 1 (18 through 45-year-olds)	1×10^9	2687	93.5% [92.3%, 94.6%]
Difference in Seroconversion Rates[d,e]			5.0% [2.8%, 6.4%]

[a] Data are derived from Study 1 (NCT02094586) and Study 5 (NCT03220737).
[b] N=number of subjects with analyzable samples at Day 1 and Day 11 in the immunogenicity evaluable population.
[c] CI=confidence interval.
[d] 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.
[e] Pre-specified success criterion was that the lower bound of the two-sided 96.7% confidence interval on the difference in seroconversion rate (Study 5 minus Study 1) must be greater than -10 percentage points. Co-primary criterion required the lower limit of the 98.3% CI to be ≥ 70% for the VAXCHORA group.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

VAXCHORA is supplied as shown in Table 8. The contents of both packets are reconstituted with **bottled** water (purified, spring, or sparkling [carbonated]), to form one oral dose of the vaccine.

Table 8: VAXCHORA Product Presentation

Presentation	Carton NDC Number	Components
Single dose carton containing two packets	NDC 50632-015-02	Buffer Component Packet NDC 50632-015-02 Active Component Packet NDC 50632-015-02

16.2 Storage and Handling

Store VAXCHORA buffer component and active component packets refrigerated at 36°F to 46°F (2°C to 8°C).

Protect from light and moisture.

Packages may be stored at 48°F to 77°F (9°C to 25°C) for no more than 24 hours prior to reconstitution.

17 PATIENT COUNSELING INFORMATION

Prior to administration of this vaccine, the health care professional should inform the individual of the following:

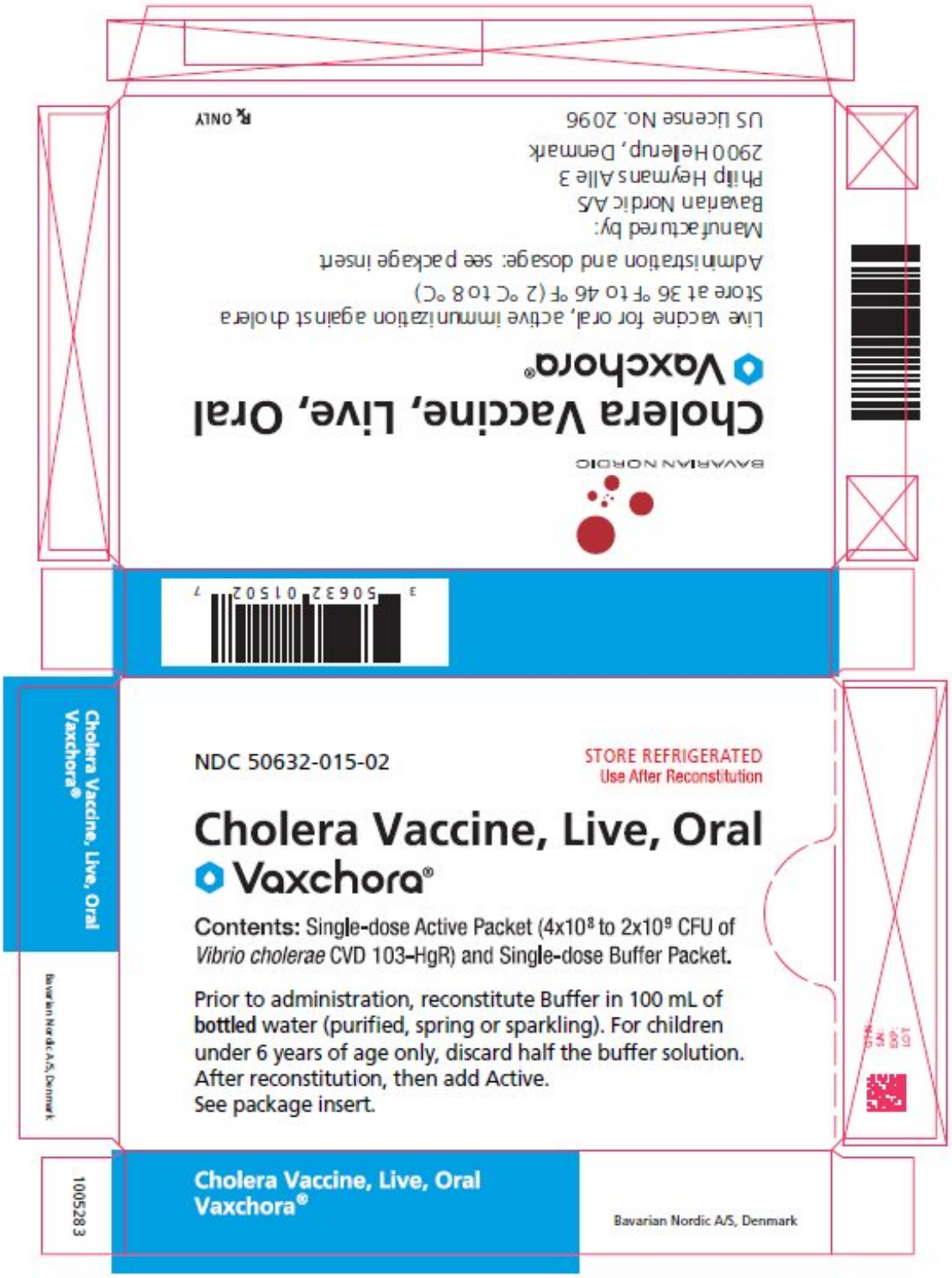
- Advise vaccine recipients to exercise caution regarding food and water consumed in cholera-affected areas, in accordance with the recommendations from the Centers for Disease Control and Prevention for the prevention of cholera in travelers.
- Educate vaccine recipients regarding the most common adverse reactions occurring within 7 days post-vaccination with VAXCHORA (tiredness, headache, abdominal pain, nausea/vomiting, lack of appetite, and diarrhea).
- Inform vaccine recipients that VAXCHORA is a live attenuated vaccine and has the potential for transmission of the vaccine strain to close contacts (e.g., household contacts). For at least 14 days following vaccination with VAXCHORA, vaccine recipients should wash their hands thoroughly after using the bathroom and before preparing or handling food.
- Instruct vaccine recipients to report adverse reactions to their healthcare provider.

VAXCHORA® is a registered trademark of Bavarian Nordic A/S

US License No. 2096

Manufactured by: Bavarian Nordic A/S, Philip Heymans Alle 3, 2900 Hellerup, Denmark

PRINCIPAL DISPLAY PANEL - Carton



Carton

NDC 50632-015-02

STORE REFRIGERATED
Use After Reconstitution

Cholera Vaccine, Live, Oral
Vaxchora®

Contents: Single-dose Active Packet (4x10^8 to 2x10^9 CFU of

Vibrio cholerae CVD 103-HgR) and Single-dose Buffer Packet.

Prior to administration, reconstitute Buffer in 100 mL of **bottled** water (purified, spring or sparkling). For children under 6 years of age only, discard half the buffer solution. After reconstitution, then add Active.
See package insert.

Cholera Vaccine, Live, Oral
Vaxchora®

Bavarian Nordic A/S, Denmark

BAVARIAN NORDIC

Cholera Vaccine, Live Oral
Vaxchora®

Live vaccine for oral, active immunization against cholera
Store at 36 °F to 46 °F (2 °C to 8 °C)

Administration and dosage: see package insert

Manufactured by:
Bavarian Nordic A/S
Philip Heymans Alle 3
2900 Hellerup, Denmark

US License No. 2096

Rx ONLY

GTIN:
S/N:
EXP:
LOT:

PRINCIPAL DISPLAY PANEL - Buffer and Active Packets

BUFFER COMPONENT
OF VAXCHORA®
(Cholera Vaccine, Live, Oral)

1

Packet 1 of 2. USE FIRST.

Contents (Single-Dose): Buffer

Directions: Add entire contents
of Packet 1 to 100 mL of **bottled**
water (purified, spring or sparkling)
in disposable cup, then stir.
For children under 6 years of age
only, discard half the buffer solution.
Go to Packet 2. See package insert.

Rx Only - For Oral Administration

EXP: LOT:

NDC 50632-015-02

Bavarian Nordic A/S

US License No. 2096

ACTIVE COMPONENT
of VAXCHORA®
(Cholera Vaccine, Live, Oral)

2

Packet 2 of 2. USE LAST.

Contents (Single-Dose):
$4x10^8$ to $2x10^9$ CFU of
lyophilized *Vibrio cholerae*
CVD 103-HgR.

Directions: Add contents of Packet 2 to cup and stir to create vaccine. See package insert.

Rx Only - For Oral Administration

EXP: LOT:

NDC 50632-015-02

Bavarian Nordic A/S
US License No. 2096

VAXCHORA

cholera vaccine, live, oral kit

Product Information			
Product Type	VACCINE	**Item Code (Source)**	NDC:50632-015

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:50632-015-02	1 in 1 CARTON; Type 0: Not a Combination Product		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 PACKET	1
Part 2	1 PACKET	1

Part 1 of 2

VAXCHORA

cholera vaccine, live, oral powder, for suspension

Product Information	
Route of Administration	ORAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
VIBRIO CHOLERAE CVD 103-HGR STRAIN LIVE ANTIGEN (UNII: V9G528E9E0) (VIBRIO CHOLERAE CVD 103-HGR STRAIN LIVE ANTIGEN - UNII:V9G528E9E0)	VIBRIO CHOLERAE CVD 103-HGR STRAIN LIVE ANTIGEN	1200000000 [CFU]

Inactive Ingredients	
Ingredient Name	**Strength**
SUCROSE (UNII: C151H8M554)	
HYDROLYZED CASEIN (ENZYMATIC; 1000 MW) (UNII: M93H91U80R)	
ASCORBIC ACID (UNII: PQ6CK8PD0R)	
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 in 1 PACKET; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125597	06/01/2024	

Part 2 of 2

BUFFER

buffer powder, for suspension

Product Information	
Route of Administration	ORAL

Inactive Ingredients	
Ingredient Name	Strength
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
SODIUM CARBONATE (UNII: 45P3261C7T)	
ASCORBIC ACID (UNII: PQ6CK8PD0R)	
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 in 1 PACKET; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125597	06/01/2024	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125597	06/01/2024	

Labeler - Bavarian Nordic A/S (310209754)

Establishment

Name	Address	ID/FEI	Business Operations
Bavarian Nordic Berna GmbH		480030654	ANALYSIS(50632-015) , LABEL(50632-015) , MANUFACTURE(50632-015) , PACK(50632-015)

Revised: 2/2025 Bavarian Nordic A/S