SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Vaxchora effervescent powder and powder for oral suspension

Cholera vaccine (recombinant, live, oral)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of vaccine contains 4 x 10^8 to 2 x 10^9 viable cells of *Vibrio cholerae* live, attenuated strain CVD 103-HgR[1].

[1] Produced by recombinant DNA technology.

This product contains genetically modified organisms (GMOs).

Excipients with known effect

Each dose of vaccine contains approximately 2.3 grams of lactose, 12.5 milligrams of sucrose, and 863 milligrams of sodium.

For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Effervescent powder and powder for oral suspension.

White-to-off-white buffer powder and white-to-beige active ingredient powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Vaxchora is indicated for active immunisation against disease caused by *Vibrio cholerae* serogroup O1 in adults and children aged 2 years and older.

This vaccine should be used in accordance with official recommendations.

4.2 Posology 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 *Vibrio cholerae* O1.

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 within 72 hours.

Revaccination

No data are available on revaccination interval.

Paediatric population

The safety and efficacy of Vaxchora in children less than 2 years has not been established. No data are available.

Method of administration

Oral use.

For instructions on reconstitution of Vaxchora prior to administration, see section 6.6.

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

The reconstituted vaccine forms a slightly cloudy suspension that may contain some white particulates. After reconstitution, the suspension should be drunk within 15 minutes. The recipient should drink the full contents of the cup at once.

4.3 Contraindications

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

Individuals with congenital immune deficiency or receiving immunosuppressive treatment.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Factors affecting protection

Vaxchora confers protection specific to *Vibrio cholerae* serogroup O1. Immunisation does not protect against *Vibrio cholerae* O139 or other species of Vibrio.

This vaccine does not provide 100% protection. Vaccinees should adhere to hygiene advice and exercise caution regarding food and water consumed in cholera-affected areas.

No data are available in persons living in cholera-affected areas or in individuals with pre-existing immunity to cholera.

The protection afforded by this vaccine may be reduced in HIV-infected individuals.

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 because protection against cholera may be diminished (see section 4.5).

Gastrointestinal Disease

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.

Limitations of the clinical data

Clinical trials were conducted in individuals age 2 to 64 years old. Efficacy was demonstrated in a human cholera challenge at 10 days or 3 months post-vaccination in adults age 18-45 years and immunobridging to other populations based on the rate of seroconversion. Immunogenicity data are available for 24 months post-vaccination (see section 5.1). There are no immunogenicity or efficacy data in individuals over 64 years of age.

Excipients

This vaccine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This vaccine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with Vaxchora, however data and clinical experience from other vaccines can be applicable to this vaccine.

Oral typhoid vaccine

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

Antibiotics

Concomitant administration of this vaccine with systemic antibiotics active against *Vibrio cholerae* should be avoided since these agents may prevent a sufficient degree of replication to occur in order to induce a protective immune response. This 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 this vaccine.

Antimalarial prophylaxis

Data from the study of a previous CVD 103-HgR-based vaccine indicate that immune responses to Vaxchora and protection against cholera may be diminished when this vaccine is administered concomitantly with chloroquine. Administer this vaccine at least 10 days before beginning antimalarial prophylaxis with chloroquine. There are no data regarding concomitant use of this vaccine with other anti-malarial drugs.

Food and drink

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

4.6 Fertility, pregnancy and lactation

Pregnancy

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

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

This vaccine should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the foetus.

Breast-feeding

It is unknown whether Vaxchora is excreted in human milk. A risk to the breastfed child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to abstain from using this vaccine taking into account the benefit of breast feeding for the child and the benefit of the vaccine for the woman.

Fertility

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

4.7 Effects on ability to drive and use machines

Vaxchora has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under Section 4.8 (e.g., fatigue, dizziness) may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of safety profile

The most frequent reported adverse reactions following Vaxchora administration are fatigue (30.2%), headache (28.3%), abdominal pain (18.4%), nausea/vomiting (17.9%), and decreased appetite (15.7%).

Tabulated summary of adverse reactions

The adverse reaction frequency classification used is as follows: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10,000 to <1/1 000); very rare (<1/10 000), not known (cannot be estimated from the available data).

Adverse Reactions	**Frequency**
Metabolism and nutrition disorders	
Decreased appetite	Very common
Nervous system disorders	
Headache	Very common
Dizziness	Uncommon
Gastrointestinal disorders	
Abdominal pain, nausea/vomiting	Very common
Diarrhoea	Common
Flatulence, constipation, abdominal distension, dyspepsia, abnormal faeces, dry mouth, eructation	Uncommon
Skin and subcutaneous tissue disorders	
Rash	Uncommon
Musculoskeletal and connective tissue disorders	
Arthralgia	Uncommon
Chills	Rare
General disorders and administration site conditions	
Fatigue	Very common
Pyrexia	Uncommon

Paediatric population

A clinical trial was conducted in 550 children age 2 to <18 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 30.2%), abdominal pain (27.8% vs 18.4%), vomiting (3.8% vs 0.2%), decreased appetite (21.4% vs 15.7%) and pyrexia (2.4% vs 0.8%).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, Cholera vaccines, ATC code: J07AE02

Mechanism of action

Vaxchora contains live attenuated cholera bacteria (*Vibrio cholerae* O1 classical Inaba strain CVD 103-HgR) that replicate in the gastrointestinal tract of the recipient and induce serum vibriocidal antibody and memory B cell responses. Immune mechanisms conferring protection against cholera following receipt of the vaccine have not been determined, however, rises in serum vibriocidal antibody 10 days after vaccination with this vaccine were associated with protection in a human challenge study.

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 vaccine or placebo recipients were challenged with live *Vibrio 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 1.

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

Parameter	Vaxchora 10 Day Challenge N=35	Vaxchora 3 Month Challenge N=33	Combined Placebo 10 Day or 3 Month Challenge N=66
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%]	-

N=number of subjects with analyzable samples

CI=confidence interval.

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 <46 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<46 years (mean age 29.9, range 18-46, 45.2% male, 54.8% female) (Study3); a trial in 398 healthy older adults age 46 to <65 years (mean age 53.8, range 46-64, 45.7% male, 54.3% female) (Study 4); and a paediatric trial in healthy subjects age 2-<18 years (Study 5). 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 <46 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 Tables 2 and 4. In the challenge study, 79.8% of subjects 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 2: Vibriocidal Antibody Seroconversion Against Classical Inaba *Vibrio cholerae* Vaccine Strain at 10 Days Post-Vaccination in Adults

Study (age in years)	Vaxchora Recipients N[b]	Vaxchora Recipients Seroconversion[a] % [95% CI]	Placebo Recipients N[b]	Placebo Recipients Seroconversion[a] % [95% CI[c]]	Immunobridging: Difference in Seroconversion Rate Compared to Study 3 in 18-45 year olds %[d] [95% CI[c]]
Challenge Trial (18 – 45)	93	90.3% [82.4%, 95.5%]	102	2.0% [0.2%, 6.9%]	-
Study 3 (18 – 45)	2687	93.5% [92.5%, 94.4%]	334	4.2% [2.3%, 6.9%]	-
Study 4 (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 <46 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 *Vibrio cholerae* are shown in Table 3. Seroconversion rates for these biotypes and serotypes were not determined in children.

Table 3: Seroconversion Rates 10 Days Post-Vaccination for the Four Major *Vibrio cholerae* O1 Serogroup Biotypes and Serotypes [Immunogenicity Evaluable Population]

Cholera Strain	Younger Adults (18 through 45 year olds) Vaxchora N[a]	Younger Adults (18 through 45 year olds) Vaxchora %[b] [95% CI[c]]	Older Adults (46 through 64 year olds) Vaxchora N[a]	Older Adults (46 through 64 year olds) Vaxchora % [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 contains the classical Inaba strain of *Vibrio cholerae* O1.

Paediatric population

An immunogenicity trial was conducted in 550 healthy children age 2 to <18 years (mean age 9.0, range 2-17, 52.0% male, 48.0% female) (study 5). 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 4.

Long-term immunogenicity data are available from a subset of children age 12 to <18 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 5.

Table 4: Vibriocidal Antibody Seroconversion Against Classical Inaba *Vibrio cholerae* Vaccine Strain at 10 Days Post-Vaccination in Children [Immunogenicity Evaluable Population]

Study (age in years)	**Vaxchora Recipients** N[b]	Seroconversion[a] % [98.3% CI]	**Placebo Recipients** N[b]	Seroconversion[a] % [95% CI[c]]	**Immunobridging: Difference in Seroconversion Rate Compared to Study 3 in 18-45 year olds** %[d] [96.7% CI]
Paediatric Trial (Study 5) (2 – <18)	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.

[c] CI=confidence interval.

[d] Non-inferiority criteria: lower bound of the two-sided 98.3% confidence interval on the difference in seroconversion rates compared with adults ages 18 to <46 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 5: Vibriocidal Antibody Seroconversion Against Classical Inaba *Vibrio cholerae* Vaccine Strain 10 through 729 Days Post-Vaccination in Children age 12 to <18 Years [Immunogenicity Evaluable Population in the Long-Term Follow-up Substudy]

Paediatric Trial (12 - < 18 years) Day Post-Vaccination	**Vaxchora** 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 in the immunogenicity evaluable population of the long term follow-up sub-study.

[c] CI=confidence interval.

MHRA has deferred the obligation to submit the results of studies with Vaxchora in one or more subsets of the paediatric population in the prevention of cholera (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No preclinical safety data are available for Vaxchora.

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

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

6.3 Shelf life

20 months.

After reconstitution, the suspension should be drunk within 15 minutes.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Store in the original package in order to protect from light and moisture.

Avoid exposure to temperatures above 25°C. Stability data indicate that the vaccine components are stable for 12 hours when stored at temperatures from 8°C to 25°C. At the end of this period Vaxchora should be used immediately or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Carton box containing one active ingredient sachet and one buffer sachet.

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

The buffer sachet contains 4.5 g of effervescent powder.

The active ingredient sachet 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 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 set of 2 sachets. One dose consists of 2 sachets (1 active ingredient sachet and 1 buffer sachet).

6.6 Special precautions for disposal and other handling

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

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

It is important to mix the sachets in the order described. First, the contents of the buffer sachet 1 (a white-to-off-white powder) are mixed with 100 mL of cold or room temperature (≤25°C) non-carbonated or carbonated bottled water in a cup. For children age 2 to <6 years ONLY, half (50 mL) of the buffer solution should then be discarded before proceeding to the next step. Second, the contents of the active component sachet 2 (a white-to-beige powder) are then added and the mixture is stirred for at least 30 seconds. The reconstituted vaccine forms a slightly cloudy suspension that may contain some white particulates. Sucrose (up to 4 g/ 1 teaspoon) or stevia sweetener (no more than 1 gram / ¼ teaspoon) may then be stirred into the suspension if desired. DO NOT add other sweeteners as this may reduce the effectiveness of the vaccine. The dose should be administered within 15 minutes of reconstitution. Some residue may remain in the cup. The cup should be washed with soap and hot water.

Note: if the sachets are reconstituted in the incorrect order, the vaccine must be discarded.

7 MARKETING AUTHORISATION HOLDER

Bavarian Nordic A/S
Philip Heymans Alle 3
DK-2900 Hellerup
Denmark

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 40365/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01/01/2021
Date of latest renewal: 09/01/2025

10 DATE OF REVISION OF THE TEXT

29/10/2025