ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS
1. NAME OF THE MEDICINAL PRODUCT

Dukoral, suspension and effervescent granules for oral suspension.
Oral cholera vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of vaccine suspension (3 ml) contains:

− A total of $1 \times 10^{11}$ bacteria of the following strains:
  - *Vibrio cholerae* O1 Inaba, classical biotype (heat inactivated) $25 \times 10^9$ bacteria*
  - *Vibrio cholerae* O1 Inaba, El Tor biotype (formalin inactivated) $25 \times 10^9$ bacteria*
  - *Vibrio cholerae* O1 Ogawa, classical biotype (heat inactivated) $25 \times 10^9$ bacteria*
  - *Vibrio cholerae* O1 Ogawa, classical biotype (formalin inactivated) $25 \times 10^9$ bacteria*

− Recombinant cholera toxin B subunit (rCTB) 1 mg
  (produced in *V. cholerae* O1 Inaba, classical biotype strain 213.)

* Bacterial count before inactivation.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Suspension and effervescent granules for oral suspension.
The suspension, supplied in a vial is whitish. The effervescent granules, supplied in a sachet, are white.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Dukoral is indicated for active immunisation against disease caused by *Vibrio cholerae* serogroup O1 in adults and children from 2 years of age who will be visiting endemic/epidemic areas.

The use of Dukoral should be determined on the basis of official recommendations taking into consideration the variability of epidemiology and the risk of contracting disease in different geographical areas and travelling conditions.

Dukoral should not replace standard protective measures. In the event of diarrhoea measures of rehydration should be instituted.

4.2 Posology and method of administration

**Posology**
The vaccine is intended for oral use. Before ingestion, the vaccine suspension should be mixed with a sodium hydrogen carbonate solution, as described below.

**Primary vaccination schedule**
The standard primary course of vaccination with Dukoral against cholera consists of 2 doses for adults and children from 6 years of age. Children 2 to 6 years of age should receive 3 doses. Doses are to be administered at intervals of at least one week. If more than 6 weeks have elapsed between doses, the primary immunisation course should be re-started.
Immunisation should be completed at least 1 week prior to potential exposure to *V. cholerae* O1.

**Booster dose**
For continuous protection against cholera a single booster dose is recommended after 2 years for adults and children from 6 years of age, and after 6 months for children aged 2 to 6 years. No clinical efficacy data has been generated on repeat booster dosing. However, immunological data suggest that if up to 2 years have elapsed since the last vaccination a single booster dose should be given. If more than 2 years have elapsed since the last vaccination the primary course should be repeated.

Dukoral has been given to children between 1 and 2 years of age in safety and immunogenicity studies, but the protective efficacy has not been studied in this age group. Therefore, Dukoral is not recommended to be used in children less than 2 years of age.

**Method of administration:**
The sodium hydrogen carbonate is supplied as effervescent granules, which should be dissolved in a glass of cool water (approx. 150 ml). The vaccine suspension should then be mixed with the sodium hydrogen carbonate solution and drunk within 2 hours. Food and drink should be avoided 1 hour before and 1 hour after vaccination. Oral administration of other medicinal products should be avoided within 1 hour before and after administration of Dukoral.

*Children 2 to 6 years of age:* half of the sodium hydrogen carbonate solution is poured away and the remaining part (approx. 75 ml) is mixed with the entire contents of the vaccine vial.

4.3 **Contraindications**

Hypersensitivity to the active substances or to any of the excipients.

Administration of Dukoral should be postponed for subjects suffering from acute gastrointestinal illness or acute febrile illness.

4.4 **Special warnings and special precautions for use**

There are only limited data on safety and immunogenicity of the vaccine in children aged 1 to 2 years and protective efficacy has not been studied. Therefore, Dukoral is not recommended to be used in children less than 2 years of age.

There are only very limited data on protective efficacy of the vaccine in subjects aged 65 years and more.

No clinical data on protective efficacy of Dukoral against cholera after administration of booster doses are available.

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

In subjects infected with HIV, limited data are available on immunogenicity and safety of the vaccine. Vaccine protective efficacy has not been studied. Immunisation of HIV infected subjects could result in transient increases of viral load. Dukoral may not induce protective antibody levels in subjects with advanced HIV disease.

Formaldehyde is used during the manufacturing process and trace amounts may be present in the final product. Caution should be taken in subjects with known hypersensitivity to formaldehyde.

The vaccine does not provide complete protection and it is important to adhere to standard protective measures to avoid cholera.
4.5 Interaction with other medicinal products and other forms of interaction

The vaccine is acid labile. Food and/or drink will increase acid production in the stomach and the effect of the vaccine may be impaired. Consequently, food and drink should be avoided 1 hour before and 1 hour after vaccination.

Oral administration of other vaccines and medicinal products should be avoided 1 hour before and 1 hour after vaccination.

Preliminary results from a clinical study including a limited number of volunteers showed no interaction with the antibody response to Dukoral when a live oral vaccine (enterocapsules) against typhoid was given simultaneously with Dukoral. The immune response to live typhoid vaccine was not investigated in this study. Similarly, a yellow fever vaccine was given concomitantly with Dukoral, and there was no observed interaction with the immune response to the yellow fever vaccine. The immune responses to Dukoral were not studied. No other vaccines/medicinal products, including oral polio vaccine and antimalarials, have been given simultaneously with Dukoral in clinical studies.

4.6 Pregnancy and lactation

No animal data on reproduction toxicity are available. Following careful benefit/risk assessment the vaccine may be administered during pregnancy and to lactating women although no specific clinical studies have been performed to address this issue.

4.7 Effects on ability to drive and use machines

No effect on the ability to drive and use machines is likely.

4.8 Undesirable effects

Adverse reactions from clinical trials

The safety of Dukoral was assessed in clinical trials, including both adults and children, conducted in endemic and non-endemic countries for cholera and enterotoxigenic Escherichia coli (ETEC) producing heat-labile enterotoxin (LT). Over 94,000 doses of Dukoral were administered during the clinical trials. Evaluation of safety varied between trials with respect to mode of surveillance, definition of symptoms and time of follow-up. In the majority of studies adverse events were assessed by passive surveillance. The most frequently reported undesirable reactions, such as gastrointestinal symptoms including abdominal pain, diarrhoea, loose stools, nausea and vomiting, occurred at similar frequencies in vaccine and placebo groups.

Uncommon (>1/1,000, <1/100): diarrhoea, abdominal pain, abdominal cramps, stomach/abdominal gurgling (gas), abdominal discomfort, headache.

Rare (>1/10,000, <1/1,000): fever, malaise, nausea, vomiting, loss of or poor appetite, respiratory symptoms (including rhinitis and cough), dizziness.

Very rare (<1/10,000): fatigue/drowsiness, dyspepsia, shivers, joint pain, sore throat, reduced sense of taste, sweating, insomnia, dehydration, fainting, rash.

Adverse reactions from post-marketing surveillance

Undesirable effects reported during post-marketing surveillance, following distribution of approximately 1,000,000 vaccine doses, are listed below.
Very rare (<1/10,000): Pain, urticaria, rash, flu-syndrome, asthenia, chills, dyspnœa, gastroenteritis, flatulence, dehydration, paraesthesia, angioedema, hypertension, increased sputum, pruritus, lymphadenitis and arthralgia.

4.9 Overdose

Data on overdose are extremely limited. Adverse reactions reported are consistent with those seen after the recommended dosing.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial vaccines, ATC-code: J07A E01

Mechanism of action

The vaccine contains killed whole \( V. \text{cholerae} \) O1 bacteria and the recombinant non-toxic B-subunit of the cholera toxin (CTB). Bacterial strains of both Inaba and Ogawa serotypes and of El Tor and Classical biotypes are included in the vaccine. Dukoral is taken orally with bicarbonate buffer, which protects the antigens from the gastric acid. The vaccine acts by inducing antibodies against both the bacterial components and CTB. The antibacterial intestinal antibodies prevent the bacteria from attaching to the intestinal wall thereby impeding colonisation of \( V. \text{cholerae} \) O1. The anti-toxin intestinal antibodies prevent the cholera toxin from binding to the intestinal mucosal surface thereby preventing the toxin-mediated diarrhoeal symptoms.

The heat-labile toxin (LT) of enterotoxigenic \( E. \text{coli} \) (ETEC ) is structurally, functionally and immunologically similar to CTB. The two toxins cross-react immunologically.

Efficacy against cholera

Efficacy against cholera was assessed in three randomised double-blind placebo-controlled clinical trials conducted in Bangladesh (endemic region) and in Peru (non-endemic region). The number of patients enrolled, dosage regimens and follow-up periods are shown in the following table.

<table>
<thead>
<tr>
<th>Study location</th>
<th>Year</th>
<th>Dosage regimen</th>
<th>Number (Age groups)</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>1985-88</td>
<td>3 doses at 6 week intervals</td>
<td>89,152</td>
<td>6 months-5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2-65 years)</td>
<td></td>
</tr>
<tr>
<td>Peru, military</td>
<td>1994</td>
<td>2 doses 7-11 days apart</td>
<td>1,563</td>
<td>5 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(18-65 years)</td>
<td></td>
</tr>
<tr>
<td>Peru, Pampas</td>
<td>1993-95</td>
<td>2 doses 2 weeks apart with a booster dose 1 year later</td>
<td>21,924</td>
<td>2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2-65 years)</td>
<td></td>
</tr>
</tbody>
</table>

In the Bangladesh field trial, protective efficacy of Dukoral in the overall population was 85% (95%CI: 56, 95, per-protocol analysis) for the initial 6 months of follow-up. Duration of vaccine protection differed by age, lasting for 6 months in children and for 2 years in adults (see table above). An exploratory analysis suggested that 2 vaccine doses seemed as effective as 3 doses in adults.
Table: Protective efficacy against cholera in the Bangladesh study (per-protocol analysis)

<table>
<thead>
<tr>
<th></th>
<th>Adults and children &gt;6 year</th>
<th>Children 2-6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>76 (30, 92)</td>
<td>100</td>
</tr>
<tr>
<td>1st year</td>
<td>76 (60, 85)</td>
<td>44 (10, 65)</td>
</tr>
<tr>
<td>2nd year</td>
<td>60 (36, 76)</td>
<td>33 (-23, 64)</td>
</tr>
</tbody>
</table>

In the second trial, conducted in Peru and enrolling military recruits, the short-term protective efficacy against cholera after 2 vaccine doses was 85% (95% CI: 36, 97, per-protocol analysis). The third study, a field trial conducted in Peru, failed to show any protective efficacy against cholera during the first year. Following a booster dose 10-12 months after primary immunisation, the protective efficacy during the second year was 60.5% (95% CI: 28, 79).

Protective efficacy of Dukoral against cholera has not been studied following repeated booster vaccination.

**Immunogenicity**

No established immunological correlates of protection against cholera after oral vaccination have been identified. There is a poor correlation between serum antibody responses, including vibriocidal antibody response, and protection. Locally produced secretory IgA antibodies in the intestine probably mediate protective immunity.

The vaccine induced intestinal antitoxin IgA responses in 70-100% of vaccinated subjects. Serum vibriocidal antibodies against the bacterial components were seen in 35-55% of vaccinated subjects and antitoxic antibodies in 78-87% of vaccinated subjects. A booster dose elicited an anamnestic response indicative of an immune memory. The duration of the immunological memory was estimated to last for at least 2 years in adults.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No preclinical safety testing with the vaccine has been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Suspension:
- Sodium dihydrogen phosphate monohydrate
- Disodium phosphate dihydrate
- Sodium chloride
- Water for injections

Effervescent granules:
- Sodium hydrogen carbonate
- Citric acid
- Sodium carbonate, anhydrous
- Saccharin sodium
- Sodium citrate
Raspberry flavour

6.2  **Incompatibilities**

Dukoral should only be mixed with the supplied effervescent granules dissolved in water.

6.3  **Shelf life**

3 years.
After the effervescent granules have been dissolved in water and the vaccine suspension has been added, the mixture should be drunk within 2 hours.

6.4  **Special precautions for storage**

Store at 2°C – 8°C (in a refrigerator). Do not freeze.

6.5  **Nature and contents of container**

The vaccine suspension is filled in a volume of 3 ml in vials (type I glass) with a rubber stopper and a screw cap.
The effervescent granules are filled in an amount of 5.6 g in sachets with an inner layer of polyester/LD-polyethylene and an outer layer of aluminium/LD-polyethylene.

Each dose of vaccine is supplied with one sachet of effervescent granules.

Pack sizes: 1x1 dose, 2x1 dose, 20x1 dose
Not all pack sizes may be marketed.

6.6  **Instructions for use and handling**

The effervescent granules should be dissolved in approximately 150 ml of cool water. The vaccine suspension should then be added to the sodium hydrogen carbonate solution and mixed well to obtain a colourless slightly opalescent solution.

*Children 2 to 6 years of age*: half of the sodium hydrogen carbonate solution is poured away and the remaining part (approx. 75 ml) is mixed with the entire contents of the vaccine vial.

Any waste material should be disposed of in accordance with local requirements.

7.  **MARKETING AUTHORISATION HOLDER**

SBL Vaccin AB
S-105 21 Stockholm
Sweden

8.  **MARKETING AUTHORISATION NUMBER(S)**

9.  **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

10.  **DATE OF REVISION OF THE TEXT**
ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION
A  MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substances

SBL Vaccin AB
SE-105 21 Stockholm
Sweden

Name and address of the manufacturer responsible for batch release

SBL Vaccin AB
SE-105 21 Stockholm
Sweden

B  CONDITIONS OF THE MARKETING AUTHORISATION

•  CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER

Medicinal product subject to medical prescription

•  OTHER CONDITIONS

The holder of this marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

Official batch release: in accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose
ANNEX III

LABELLING AND PACKAGE LEAFLET
A. LABELLING
1. NAME OF THE MEDICINAL PRODUCT

DUKORAL, suspension and effervescent granules for oral suspension. Oral cholera vaccine

2. STATEMENT OF ACTIVE SUBSTANCES

Active substances: 1 dose contains
- \(25 \times 10^9\) bacteria* of each of the following \(V.\) cholerae O1 strains: Inaba classical biotype (heat inactivated), Inaba El Tor biotype (formalin inactivated), Ogawa classical biotype (heat inactivated), Ogawa classical biotype (formalin inactivated).
- Recombinant cholera toxin B subunit (rCTB) 1 mg.

*bacterial content prior to inactivation

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

3 ml of suspension in a vial and 5.6 g of effervescent granules in a sachet. 1 dose

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Exp MM/YYYY

9. SPECIAL STORAGE CONDITIONS
Store at 2 °C – 8 °C (in a refrigerator).  
Do not freeze.

<table>
<thead>
<tr>
<th>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</th>
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<tr>
<th>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</th>
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SBL Vaccin AB  
105 21 Stockholm, Sweden

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<th>12. MARKETING AUTHORISATION NUMBER(S)</th>
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<tr>
<th>13. MANUFACTURER’S BATCH NUMBER</th>
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Lot

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<tr>
<th>14. GENERAL CLASSIFICATION FOR SUPPLY</th>
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</table>
Medicinal product subject to medical prescription.

<table>
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<tr>
<th>15. INSTRUCTIONS ON USE</th>
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</thead>
</table>
**Instructions**  
1. Dissolve the effervescent granules in a glass of cool water (approx. 150 ml).  
   *Children 2-6 years: pour away half of the solution.*  
2. Shake the vaccine vial (1 vial = 1 dose).  
3. Add the vaccine to the sodium hydrogen carbonate solution. Mix well and drink the mixture.
PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING

Dukoral – 2x1 dose package

1. NAME OF THE MEDICINAL PRODUCT

DUKORAL, suspension and effervescent granules for oral suspension.
Oral cholera vaccine

2. STATEMENT OF ACTIVE SUBSTANCES

Active substances: 1 dose contains
- 25x10^9 bacteria* of each of the following V. cholerae O1 strains: Inaba classical biotype (heat inactivated), Inaba El Tor biotype (formalin inactivated), Ogawa classical biotype (heat inactivated), Ogawa classical biotype (formalin inactivated).
- Recombinant cholera toxin B subunit (rCTB) 1 mg.

*bacterial content prior to inactivation

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

3 ml of suspension in a vial and 5.6 g of effervescent granules in a sachet.
2x1 dose

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Exp MM/YYYY

9. SPECIAL STORAGE CONDITIONS
Store at 2 °C – 8 °C (in a refrigerator).
Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

SBL Vaccin AB
105 21 Stockholm, Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. MANUFACTURER’S BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

Instructions
1. Dissolve the effervescent granules in a glass of cool water (approx. 150 ml).
   Children 2-6 years: pour away half of the solution.
2. Shake the vaccine vial (1 vial = 1 dose).
3. Add the vaccine to the sodium hydrogen carbonate solution. Mix well and drink the mixture.
PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING

Dukoral – 20x1 dose package (outer sleeve)

1. **NAME OF THE MEDICINAL PRODUCT**

DUKORAL, suspension and effervescent granules for oral suspension.
Oral cholera vaccine

2. **STATEMENT OF ACTIVE SUBSTANCES**

Active substances: 1 dose contains
- $25 \times 10^9$ bacteria* of each of the following *V. cholerae* O1 strains: Inaba classical biotype (heat inactivated), Inaba El Tor biotype (formalin inactivated), Ogawa classical biotype (heat inactivated), Ogawa classical biotype (formalin inactivated).
- Recombinant cholera toxin B subunit (rCTB) 1 mg.

*bacterial content prior to inactivation

3. **LIST OF EXCIPIENTS**

4. **PHARMACEUTICAL FORM AND CONTENTS**

3 ml of suspension in a vial and 5.6 g of effervescent granules in a sachet.
20x1 dose

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

For oral use.

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN**

Keep out of the reach and sight of children.

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

8. **EXPIRY DATE**

Exp MM/YYYY

9. **SPECIAL STORAGE CONDITIONS**
Store at 2 °C – 8 °C (in a refrigerator).
Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER
SBL Vaccin AB
105 21 Stockholm, Sweden

12. MARKETING AUTHORISATION NUMBER(S)
EU/0/00/000/000

13. MANUFACTURER’S BATCH NUMBER
Lot

14. GENERAL CLASSIFICATION FOR SUPPLY
Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

Instructions
1. Dissolve the effervescent granules in a glass of cool water (approx. 150 ml).
   Children 2-6 years: pour away half of the solution.
2. Shake the vaccine vial (1 vial = 1 dose).
3. Add the vaccine to the sodium hydrogen carbonate solution. Mix well and drink the mixture.
1. NAME OF THE MEDICINAL PRODUCT

DUKORAL, suspension
Oral cholera vaccine

2. STATEMENT OF ACTIVE SUBSTANCES

Active substances: 1 dose contains
- $25 \times 10^9$ bacteria* of each of the following *V. cholerae* O1 strains: Inaba classical biotype (heat inactivated), Inaba El Tor biotype (formalin inactivated), Ogawa classical biotype (heat inactivated), Ogawa classical biotype (formalin inactivated).
- Recombinant cholera toxin B subunit (rCTB) 1 mg.

* bacterial content prior to inactivation

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

20x1 dose

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Exp MM/YYYY

9. SPECIAL STORAGE CONDITIONS
Store at 2 °C – 8 °C (in a refrigerator).
Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

SBL Vaccin AB
105 21 Stockholm, Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. MANUFACTURER’S BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE
**PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING**

Dukoral – 20x1 dose package (inner carton for 20 sodium hydrogen carbonate sachets)

---

1. **NAME OF THE MEDICINAL PRODUCT**

SODIUM HYDROGEN CARBONATE
Effervescent granules

---

2. **STATEMENT OF ACTIVE SUBSTANCES**

---

3. **LIST OF EXCIPIENTS**

---

4. **PHARMACEUTICAL FORM AND CONTENTS**

20 x 5.6 g

---

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

To be used with Dukoral.
For oral use.
Read the package leaflet before use.

---

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN**

Keep out of the reach and sight of children.

---

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**

---

8. **EXPIRY DATE**

Exp MM/YYYY

---

9. **SPECIAL STORAGE CONDITIONS**

---

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

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<table>
<thead>
<tr>
<th>11.</th>
<th>NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</th>
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<tbody>
<tr>
<td></td>
<td>SBL Vaccin AB</td>
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<td></td>
<td>105 21 Stockholm, Sweden</td>
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<td>GENERAL CLASSIFICATION FOR SUPPLY</td>
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<tr>
<td>15.</td>
<td>INSTRUCTIONS ON USE</td>
</tr>
</tbody>
</table>
**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

Dukoral, vial label 1 dose

1. **NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

   DUKORAL
   Suspension for oral use.

2. **METHOD OF ADMINISTRATION**

   Read the package leaflet before use.

3. **EXPIRY DATE**

   Exp MM/YYYY

4. **BATCH NUMBER**

   Lot

5. **CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

   1 dose (3 ml)
**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

Sodium hydrogen carbonate 5.6 g, sachet

---

1. **NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Sodium hydrogen carbonate  
Effervescent granules for oral use

2. **METHOD OF ADMINISTRATION**

To be used with Dukoral.  
Read the package leaflet before use.

3. **EXPIRY DATE**

Exp MM/YYYY

4. **BATCH NUMBER**

Lot

5. **CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

5.6 g

SBL Vaccin AB, Sweden
B. PACKAGE LEAFLET
PACKAGE LEAFLET

Read all of this leaflet carefully before you start using this vaccine.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This vaccine has been prescribed for you personally and you should not pass it on to others.

In this leaflet:
1. What Dukoral is and what it is used for
2. Before you use Dukoral
3. How to use Dukoral
4. Possible side effects
5. Storing Dukoral

DUKORAL, suspension and effervescent granules for oral suspension
Oral cholera vaccine

- The active substances are:
  25x10^9 bacteria* of each of the following V. cholerae O1 strains: Inaba classical biotype (heat inactivated), Inaba El Tor biotype (formalin inactivated), Ogawa classical biotype (heat inactivated), Ogawa classical biotype (formalin inactivated).
  Recombinant cholera toxin B subunit (rCTB) 1 mg.
  *bacterial content prior to inactivation

- The other ingredients in the vaccine suspension are sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium chloride and water for injections.

- The effervescent granules contain sodium hydrogen carbonate, citric acid, sodium carbonate, saccharin sodium, sodium citrate and raspberry flavour.

Marketing Authorisation Holder and manufacturer:
SBL Vaccin AB, 105 21 Stockholm, Sweden.

1. WHAT DUKORAL IS AND WHAT IT IS USED FOR

Dukoral is an oral vaccine that stimulates the immunological defence in the gut. The vaccine protects adults and children from 2 years of age against cholera

The vaccine is a whitish suspension supplied in a vial. The sodium hydrogen carbonate is white effervescent granules with a raspberry flavour supplied in a sachet.

Dukoral is available in packs of 1, 2 and 20 doses.
2. BEFORE YOU USE DUKORAL

Do not use Dukoral:
- if you are allergic to any ingredient of the vaccine.
- if you have an acute stomach disorder or infection with fever (vaccination should be delayed).

Take special care with Dukoral:
- if you are allergic to formaldehyde.

Using Dukoral with food and drink:
Avoid food and drink 1 hour before and 1 hour after the vaccination.

Pregnancy
Ask your doctor or pharmacist for advice before taking any medicine.

Breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
The vaccine is unlikely to produce an effect on the ability to drive and use machines.

Using other medicines:
Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.

3. HOW TO USE DUKORAL

Adults and children from 6 years of age: The primary vaccination is 2 doses. Doses are to be taken with an interval of 1 to 6 weeks. For continuous protection, re-vaccination is recommended after 2 years. If up to 2 years have passed since the last vaccination a single dose is sufficient. If more than 2 years have passed since the last vaccination, the primary vaccination (2 doses) should be repeated.

Children of 2 to 6 years of age: The primary vaccination is 3 doses. Doses are to be taken with an interval of 1 to 6 weeks. For continuous protection, re-vaccination is recommended after 6 months. If up to 2 years have passed since the last vaccination a single dose is sufficient. If more than 2 years have passed since the last vaccination, the primary vaccination (3 doses) should be repeated.

Protection against cholera can be expected about 1 week after the primary vaccination is completed.

The vaccine does not provide complete protection and it is important to adhere to dietary and hygiene advice to avoid diarrhoeal diseases.
Instructions:

1. Dissolve the effervescent granules in a glass of cool water (approx. 150 ml).  
   *Children 2-6 years: pour away half of the solution.*

2. Shake the vaccine vial (1 vial = 1 dose).

3. Add the vaccine to the sodium hydrogen carbonate solution. Mix well and 
   drink the mixture.

4. **POSSIBLE SIDE EFFECTS**

   Like all medicines, Dukoral can have side effects.

   Uncommon side effects (reported by less than 1 in a 100 but more than 1 in a 1,000 people) include: diarrhoea, stomach pain, stomach cramps, gurgling stomach, bloated stomach, stomach gas and general stomach discomfort, headache

   Rare side effects (reported by less than 1 in a 1,000 but more than 1 in a 10,000 people) include: high temperature, generally feeling unwell, nausea, vomiting, loss of /or poor appetite, runny nose, cough and dizziness.

   Very rare side effects (reported by less than 1 in a 10,000 people) include: fatigue/feeling tired, shivering, severe diarrhoea, joint pain, sore throat, reduced sense of taste, sweating, being unable to sleep, general pain, hives or nettle rash, other types of rashes, flu-like symptoms, weakness, feeling cold, breathlessness, pins and needles, dehydration (loss of water from the body), swelling of face, high blood pressure, chestiness, itching, and swelling of the lymph glands.

   If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. **STORING DUKORAL**

   Keep out of the reach and sight of children.

   Store at 2°C – 8°C (in a refrigerator). Do not freeze.

   Do not use after the expiry date stated on the carton.

   Drink the vaccine within 2 hours after mixing with the sodium hydrogen carbonate solution.

**This leaflet was last approved on**