ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Entericolix, emulsion for injection for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (2ml) of the inactivated vaccine contains:

Active substances:

Escherichia coli strain P4 (F6 adhesins),	≥ 1 RP *
Escherichia coli strain P5 (F18ab adhesins),	≥ 1 RP *
Escherichia coli strain P6 (F4ac adhesins),	≥ 1 RP *
Escherichia coli strain P9 (F18ac adhesins),	≥ 1 RP *
Escherichia coli strain P10 (F5 + F41 adhesins),	≥ 1 RP *
beta toxoid of *Clostridium perfringens* type C (CZV13)	≥ 10 IU** of β antitoxin/ml of rabbit serum

* RP: Relative potency for each antigen according to a reference vaccine with satisfactory result in the immunogenicity test (Ph. Eur. monograph 0962).
** IU: International units of beta toxin (Ph. Eur. monograph 0363)

Adjuvant:

Light mineral oil	0.760 ml
Montanide 103	0.0425 ml
Sorbitan oleate	0.0425 ml

Excipients:

Thiomersal	0.2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Emulsion for injection
Milky white homogenous emulsion

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (sows and gilts for reproduction).

4.2 Indications for use, specifying the target species

Vaccination of sows and gilts for the passive immunization of piglets against colibacillosis caused by enteropathogenic and enterotoxigenic *E. coli* strains expressing F4ac, F5, F6, F18ac and F41 adhesins, against oedema disease caused by *E. coli* strain expressing F18ab adhesin and against necrotic enteritis caused by *C. perfringens* type C.

Neonatal piglets

- The vaccine reduces mortality and clinical signs (severe diarrhoea) due to colibacillosis.
- The vaccine reduces mortality and clinical signs due to necrotic enteritis caused by *C. perfringens* type C.

Weaned piglets

- The vaccine reduces mortality and clinical signs due to oedema disease
- The vaccine reduces clinical signs (severe diarrhoea) of colibacillosis
- The vaccine reduces clinical signs of chronic enteritis due to *C. perfringens* type C

Duration of immunity:

– 21 days for infections caused by F4ac, F18ac, (colibacillosis) and *Clostridium perfringens* type C (necrotic enteritis)
– 21 days for antibodies against F5, F6 and F41, however the protective efficacy of the antibody levels was not established
– 28 days for infections caused by F18ab (oedema disease)

4.3 Contraindications

Do not use in case of hypersensitivity to the active substances, to the adjuvants or to any of the excipients

4.4 Special warnings for each target species

Vaccinate healthy animals only.

4.5 Special precautions for use

Special precautions for use in animals

Not applicable

Special precautions to be taken by the person administering the veterinary medicinal product to animals

To the user:
This veterinary medicinal product contains mineral oil. Accidental injection/self injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again.

To the physician:
This veterinary medicinal product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert, PROMPT, surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon.

4.6 Adverse reactions (frequency and seriousness)

A transient increase in body temperature (maximum 2ºC) can be observed between 4–24 hours after vaccination, this event is very common. Temperatures return to normal values within 24–48 hours.

The vaccine can produce short term apathy between 1 and 2 days post-vaccination, this event is common. Apathy may last for up to 7 days after vaccination, however this event is uncommon.

Injection site reactions (swelling and reddening) occurred rarely, with a maximum of 3 cm of diameter and a maximum of 10 days of duration.

Anaphylactic reactions (which may be fatal) have been reported very rarely.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy.

The vaccine should not be given in the 4 week period before the expected farrowing date.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case-by-case basis.

4.9 Amounts to be administered and administration route

Intramuscular use.

Shake vigorously before use and at intervals during use.
Avoid introduction of contamination during use.

Doses
Sows and gilts: 2 ml.

Before use, allow the vaccine to reach room temperature and shake the bottle vigorously. Inoculate the corresponding dose by deep intramuscular injection in the neck muscles. It is very important to use needles of appropriate length according to the weight of the animal.
It is recommended that the second dose should be given preferably on the alternate side.

Vaccination schedule
Pregnant sows: The initial course consists of two doses. Administer one dose 7 weeks before farrowing followed by a second dose 4 weeks before farrowing. Revaccinate with a single dose 4 weeks before farrowing in subsequent gestation periods.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

After administration of a double vaccine dose, a slightly higher transient temperature increase may be observed compared to that after a single vaccine dose (e.g. temperature increase of up to 2.5 ºC after a double dose).

4.11 Withdrawal period

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Inactivated bacterial vaccines against *Escherichia coli* and *Clostridium perfringens*.

ATC vet code. QI09AB08

The vaccine contains inactivated strains of *Escherichia coli* expressing the adhesins F4ac, F5, F6, F18ab, F18ac and F41 which cause neonatal enterotoxicosis in piglets, as well as β-enterotoxin from *Clostridium perfringens* type C. The vaccine is formulated with an oily adjuvant. In sows and gilts, the vaccine induces the specific seroconversion of vaccinated animals; piglets are passively immunised by intake of colostrum containing *Escherichia coli* adhesin-specific and *Clostridium perfringens* anti-enterotoxin antibodies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate, anhydrous
Formaldehyde
Light mineral oil
Montanide 103
Thiomersal
Polysorbate 80
Potassium dihydrogen phosphate
Sodium chloride
Sorbitan oleate
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening of the immediate packaging: 10 hours.

6.4 Special precautions for storage

Store and transport refrigerated (2 ºC – 8 ºC). Protect from light . Do not freeze.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 multi-dose high-density polyethylene (HDPE) bottle of 50 ml (25 doses) with a perforable nitrile rubber stopper and aluminium seal.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra
Spain

8. MARKETING AUTHORISATION NUMBER

To be completed nationally.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27/01/2016
Date of last renewal: 06/10/2020

10 DATE OF REVISION OF THE TEXT

06/2023

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Entericolix, emulsion for injection for pigs

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

One dose (2ml) of the vaccine contains:

-Inactivated E. coli strains expressing the adhesins F6 (P987), F18ab and F18 ac, F4ac (K88ac), F5 (K99) and F41 ≥ 1 RP
-beta toxoid of *C. perfringens* type C ≥ 10 IU
Adjuvant**:** Light mineral oil (0.760 ml), Montanide 103 (0.0425 ml), Sorbitan oleate (0.0425 ml); Preservative**:** Thiomersal (0.2 mg).

3. PHARMACEUTICAL FORM

Emulsion for injection

4. PACKAGE SIZE

50 ml (25 doses)

5. TARGET SPECIES

Pigs

6. INDICATION(S)

Read the package leaflet before use.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Deep IM use

8. WITHDRAWAL PERIOD

Withdrawal period: zero days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Accidental self-injection is dangerous.

10. EXPIRY DATE

EXP {month/year}
Once broached use within 10 hours.

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated. Do not freeze. Protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CZ Vaccines S.A.U.
36410 O Porriño – Spain

16. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottles of 50 ml (25 doses)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Entericolix, emulsion for injection for pigs

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

One dose (2 ml) contains:
Inactivated *E. coli* strains expressing F6 (P987), F18ab and F18ac, F4ac (K88ac), F5 (K99), F41 and beta toxoid of *C. perfringens* type C.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

50 ml (25 doses)

4. ROUTE(S) OF ADMINISTRATION

Deep IM use

5. WITHDRAWAL PERIOD

Withdrawal period: zero days.

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}
Once broached use within 10 hours.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Entericolix emulsion for injection for pigs

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release
CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Entericolix emulsion for injection for pigs

3. STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENTS

One dose (2 ml) of the inactivated vaccine contains:

Active substances:

Escherichia coli strain P4 (F6 adhesins),	≥ 1 RP *
Escherichia coli strain P5 (F18ab adhesins),	≥ 1 RP *
Escherichia coli strain P6 (F4ac adhesins),	≥ 1 RP *
Escherichia coli strain P9 (F18ac adhesins),	≥ 1 RP *
Escherichia coli strain P10 (F5 + F41 adhesins),	≥ 1 RP *
beta toxoid of *Clostridium perfringens* Type C (CZV13)	≥ 10 IU** of β antitoxin/ml of rabbit serum

* RP: Relative potency for each antigen according to a reference vaccine with satisfactory result in the immunogenicity test (Ph. Eur. monograph 0962).
** IU: International units of beta toxin (Ph. Eur. monograph 0363)

Adjuvant:

Light mineral oil	0.760 ml
Montanide 103	0.0425 ml
Sorbitan oleate	0.0425 ml

Excipients:

Thiomersal	0.2 mg

Milky white homogenous emulsion for injection

4. INDICATIONS

Vaccination of sows and gilts for the passive immunization of piglets against colibacillosis caused by enteropathogenic and enterotoxigenic *E. coli* strains expressing F4ac, F5, F6, F18ac and F41 adhesins, against oedema disease caused by *E. coli* strain expressing F18ab adhesin and against necrotic enteritis caused by *C. perfringens* type C.

Neonatal piglets
- The vaccine reduces mortality and clinical signs (severe diarrhoea) due to colibacillosis.
- The vaccine reduces mortality and clinical signs due to necrotic enteritis caused by *C. perfringens* type C.

Weaned piglets
- The vaccine reduces mortality and clinical signs due to oedema disease.
- The vaccine reduces clinical signs (severe diarrhoea) of colibacillosis.
- The vaccine reduces clinical signs of chronic enteritis due to *C. perfringens* type C.

Duration of immunity
– 21 days for infections caused by F4ac, F18ac (colibacillosis) and *Clostridium perfringens* type C (necrotic enteritis).
– 21 days for antibodies against F5, F6 and F41, however the protective efficacy of the antibody levels was not established.
– 28 days for infections caused by F18ab (oedema disease).

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substances, to the adjuvants or to any of the excipients

6. ADVERSE REACTIONS

A transient increase in body temperature (maximum 2ºC) can be observed between 4–24 hours after vaccination, this event is very common. Temperatures return to normal values within 24–48 hours.

The vaccine can produce short term apathy between 1 and 2 days post-vaccination, this event is common. Apathy may last for up to 7 days after vaccination, however this event is uncommon.

Injection site reactions (swelling and reddening) occurred rarely, with a maximum of 3 cm of diameter and a maximum of 10 days of duration.

Anaphylactic reactions, a severe form of allergic reaction which may be fatal, have been reported very rarely.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs (sows and gilts for reproduction).

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Deep intramuscular use

Doses
Sows and gilts: 2 ml.

Vaccination schedule
Pregnant sows: The initial course consists of two doses. Administer one dose 7 weeks before farrowing followed by a second dose 4 weeks before farrowing. Revaccinate with a single dose 4 weeks before farrowing in subsequent gestating periods.

9. ADVICE ON CORRECT ADMINISTRATION

Before use, allow the vaccine to reach room temperature and shake the bottle vigorously. Inoculate the corresponding dose by deep intramuscular injection in the neck muscles. It is very important to use needles of appropriate length according to the weight of the animal.
It is recommended that the second dose should be given preferably on the alternate side.

Shake vigorously before use and at intervals during use.
Avoid introduction of contamination during use.

10. WITHDRAWAL PERIOD

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store and transport refrigerated (2 ºC – 8 ºC).
Protect from light .
Do not freeze.
Shelf life after first opening the container: 10 hours.
Do not use this veterinary medicinal product after the expiry date (EXP) which is stated on the carton and the bottle.

12. SPECIAL WARNINGS

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

To the user:
This veterinary medicinal product contains mineral oil. Accidental injection/self injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again.

To the physician:
This veterinary medicinal product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert, PROMPT, surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon.

Pregnancy and lactation
Can be used during pregnancy.

The vaccine should not be given in the 4 week period before the expected farrowing date.

Interaction with other medicinal products and other forms of interaction:
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case-by-case basis.

Overdose (symptoms, emergency procedures, antidotes):
After administration of a double vaccine dose, a slightly higher transient temperature increase may be observed compared to that after a single vaccine dose (e.g. temperature increase of up to 2.5 ºC after a double dose).

Incompatibilities
In the absence of compatibility studies this veterinary medicinal product must not be mixed with other veterinary medicinal products.

13. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

06/2023

15. OTHER INFORMATION

Pharmacotherapeutic group: Inactivated bacterial vaccines against *Escherichia coli* and *Clostridium perfringens*.

ATC vet code. QI09AB08

The vaccine contains inactivated strains of *Escherichia coli* expressing the adhesins F4ac, F5, F6, F18ab, F18ac and F41 which cause neonatal enterotoxicosis in piglets, as well as β-enterotoxin from *Clostridium perfringens* type C. The vaccine is formulated with an oily adjuvant. In sows and gilts, the vaccine induces the specific seroconversion of vaccinated animals; piglets are passively immunised by intake of colostrum containing *Escherichia coli* adhesin-specific and *Clostridium perfringens* anti-enterotoxin antibodies.

For animal treatment only
To be supplied on veterinary prescription.

Register MA No:
To be completed nationally, if needed.

Pack size:
Cardboard box with 1 bottle of 50 ml (25 doses) of the vaccine.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.