

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18 lyophilisate for oral suspension for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of vaccine contains:

Active substances:

Live non-pathogenic *Escherichia coli* O8:K87* (F4ac):.....1.3x10⁸ to 9.0x10⁸ CFU**

Live non-pathogenic *Escherichia coli* O141:K94* (F18ac):2.8x10⁸ to 3.0x10⁹ CFU**

* not attenuated

**CFU – colony forming units

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilisate for oral suspension.

White or whitish powder.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs.

4.2 Indications for use, specifying the target species

For active immunisation of pigs from 18 days of age against enterotoxigenic F4-positive and F18-positive *Escherichia coli* in order to:

- reduce the incidence of moderate to severe post-weaning *E. coli* diarrhoea (PWD) in infected pigs;
- reduce the faecal shedding of enterotoxigenic F4-positive and F18-positive *E. coli* from infected pigs.

Onset of immunity: 7 days after vaccination

Duration of immunity: 21 days after vaccination

4.3 Contraindications

None.

4.4 Special warnings for each target species

It is not recommended to vaccinate animals undergoing immunosuppressive treatment or to vaccinate animals undergoing antibacterial treatment effective against *E. coli*.

Vaccinate healthy animals only.

4.5 Special precautions for use

Special precautions for use in animals

The vaccine strains may be excreted by vaccinated piglets for at least 14 days following vaccination. The vaccine strains readily spread to other pigs in contact to vaccinated pigs. Unvaccinated pigs in contact with vaccinated pigs will harbour and shed the vaccine strains similarly to vaccinated pigs. During this time, the contact of immunosuppressed pigs with vaccinated pigs should be avoided.

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

Personal protective equipment consisting of protective disposable gloves and safety glasses should be worn when handling the veterinary medicinal product.

In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician. In case of spillage onto skin, rinse with water and seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

No adverse reactions have been observed.

4.7 Use during pregnancy, lactation or lay

The use is not recommended during pregnancy.

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

Oral use.

Vaccination schedule: administer a single dose orally from 18 days of age.

All materials used in preparing and administering the vaccine must be free of antimicrobials, detergent or disinfectant residues to prevent inactivation.

The reconstituted vaccine is a transparent to opaque white-yellowish suspension depending on the volume of water used for dilution.

Vaccination by drench application:

- 50-dose presentation: Reconstitute the lyophilisate by adding 10 ml of water to the vial. Shake well and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 100 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.
- 200-dose presentation: Reconstitute the lyophilisate by adding 20 ml of water to the vial. Shake well and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 400 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.

Vaccination via the drinking water system:

The drinking water systems have to be cleaned and intensively rinsed with untreated water to avoid any residues of antimicrobials, detergents or disinfectants.

Withhold drinking water supply for 1 to 2 hours prior to the planned vaccination to stimulate drinking of the vaccine suspension.

Reconstitute the lyophilisate by adding 10 ml (50-dose presentation) or 20 ml (200-dose presentation) of water to the vial. Shake well.

The final suspension containing the vaccine should be consumed within 4 hours after preparation. Provide enough space so that all pigs can drink the required amount. The actual amount of water consumed may however vary considerably depending on several factors. Therefore, it is recommended to assess the actual water intake during a 4-hour time period the day before vaccination. Alternatively, refer to the following table:

Body weight (kg)	Water consumption (litres) in a 4-hour time period		
	1 pig	50 pigs	200 pigs
Up to 4.5	0.11 litres	5.5 litres	22 litres
4.6 to 6.8	0.17 litres	8.5 litres	34 litres
6.9 to 9.0	0.23 litres	11.5 litres	46 litres

- For administration using bowls or tanks, dilute the reconstituted vaccine in the volume of water that the pigs will drink during a 4-hour time period.
- For administration through water lines using a dosing pump (proportioner), dilute the reconstituted vaccine in the needed volume of the dosing pump stock solution. The volume of stock solution is calculated using the volume of water that the pigs will drink during a 4-hour time period multiplied by the dosing pump rate (in decimal). As an example, for a 4-hour consumption of 22 litres and a dosing pump rate of 1%, the volume of the stock solution should be $22 \text{ litres} \times 0.01 = 220 \text{ ml}$.

In case of concerns about the presence of disinfectant residues in the drinking water, such as chlorine, it is recommended to add skimmed milk powder as a stabilizer into the drinking water prior to adding the vaccine. The final concentration of the skimmed milk powder should be 5 g/litre.

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

A rectal temperature up to 41.2 °C may occur in individual animals within the first 24 hours after administration of a 10-fold overdose.

4.11 Withdrawal period(s)

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Immunologicals for Suidae; live bacterial vaccine.
ATCvet code: QI09AE03.

To stimulate active immunity against enterotoxigenic F4-positive and F18-positive *E. coli* in pigs.

The vaccine induces an intestinal immunity and a serological response against F4-positive and F18-positive *E. coli* in pigs. The vaccine confers cross protection against F18ab-positive *E. coli*, as demonstrated by challenge for both the 7-day onset of immunity and the 21-day duration of immunity. Antibodies triggered by the vaccine provide cross-reactivity against F4ab and F4ad-positive *E. coli* strains.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextran 40,000
Sucrose
Monosodium glutamate
Purified water

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after reconstitution and dilution according to directions: 4 hours.

6.4. Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C).
Protect from light.

6.5 Nature and composition of immediate packaging

Type I glass vial of 11 ml containing 50 doses and type II glass vial of 50 ml containing 200 doses with a chlorobutyl rubber stopper sealed with an aluminium cap.

Cardboard box of one vial of 50 or 200 doses.
Cardboard box of four vials of 50 doses.

Not all pack sizes may be marketed.

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/16/202/001-003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09/01/2017
Date of last renewal:

10 DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

- A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. STATEMENT OF THE MRLs**

**A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND
MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer of the biological active substances:

CZ Veterinaria S.A.
Poligono La Relva, Torneiros s/n
36410 Porriño (Pontevedra)
SPAIN

Name and address of the manufacturer responsible for batch release:

Klifovet AG
Geyerspergerstr. 27
80689 München
GERMANY

Lohmann Animal Health GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

The active substances being principles of biological origin intended to produce immunity is not within the scope of Regulation (EC) No 470/2009.

The excipients listed in section 6.1 of the SPC are either allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18 lyophilisate for oral suspension for pigs

2. STATEMENT OF ACTIVE SUBSTANCES

Live non-pathogenic <i>E. coli</i> O8:K87 (F4ac):	1.3x10 ⁸ to 9.0x10 ⁸ CFU/dose
Live non-pathogenic <i>E. coli</i> O141:K94 (F18ac):	2.8x10 ⁸ to 3.0x10 ⁹ CFU/dose

3. PHARMACEUTICAL FORM

Lyophilisate for oral suspension

4. PACKAGE SIZE

1 x 50 doses
4 x 50 doses
1 x 200 doses

5. TARGET SPECIES

Pigs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s): zero days

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated.
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

Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/16/202/001-003

17. MANUFACTURER’S BATCH NUMBER

Lot.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vials (50 or 200 doses)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18 lyophilisate for oral suspension for pigs

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Live *E. coli* O8:K87 (F4ac) and live *E. coli* O141:K94 (F18ac)

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

50 doses
200 doses

4. ROUTE(S) OF ADMINISTRATION

Oral use

5. WITHDRAWAL PERIOD(S)

Withdrawal period(s): zero days

6. BATCH NUMBER

Lot

7. EXPIRY DATE

EXP

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Coliprotec F4/F18 lyophilisate for oral suspension 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:

Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

Manufacturer responsible for batch release:

Klifovet AG
Geyerspergerstr. 27
80689 München
GERMANY

Lohmann Animal Health GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
GERMANY

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Coliprotec F4/F18 lyophilisate for oral suspension for pigs

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each dose of vaccine contains:

Live non-pathogenic *E. coli* O8:K87* (F4ac):.....1.3x10⁸ to 9.0x10⁸ CFU**
Live non-pathogenic *E. coli* O141:K94* (F18ac):.....2.8x10⁸ to 3.0x10⁹ CFU**

* not attenuated

**CFU – colony forming units

White or whitish powder.

4. INDICATION(S)

For active immunisation of pigs from 18 days of age against enterotoxigenic F4-positive and F18-positive *E. coli* in order to:

- reduce the incidence of moderate to severe post-weaning *E. coli* diarrhoea (PWD) in infected pigs;
- reduce the faecal shedding of enterotoxigenic F4-positive and F18-positive *E. coli* from infected pigs.

Onset of immunity: 7 days after vaccination

Duration of immunity: 21 days after vaccination

5. CONTRAINDICATIONS

None

6. ADVERSE REACTIONS

No adverse reactions have been observed.

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

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

Oral use.

Administer a single dose of vaccine from 18 days of age.

9. ADVICE ON CORRECT ADMINISTRATION

All materials used in preparing and administering the vaccine must be free of antimicrobials, detergent or disinfectant residues to prevent inactivation.

Vaccination schedule: administer a single dose orally from 18 days of age.

The reconstituted vaccine is transparent to opaque white-yellowish suspension depending on the volume of water used for dilution.

Vaccination by drench application:

- 50-dose presentation: Reconstitute the lyophilisate by adding **10 ml** of water to the vial. **Shake well** and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 100 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.
- 200-dose presentation: Reconstitute the lyophilisate by adding **20 ml** of water to the vial. **Shake well** and transfer the suspension into a graduated container, mix again with water to complete to a total volume of 400 ml. Shake well and use within 4 hours. Administer a single 2 ml dose orally to pigs, irrespective of body weight.

Vaccination via the drinking water system:

The drinking water systems have to be cleaned and intensively rinsed with untreated water to avoid any residues of antimicrobials, detergents or disinfectants.

Withhold drinking water supply for 1 to 2 hours prior to the planned vaccination to stimulate drinking of the vaccine suspension.

Reconstitute the lyophilisate by adding **10 ml** (50-dose presentation) or **20 ml** (200-dose presentation) of water to the vial. **Shake well**.

The final suspension containing the vaccine should be consumed within 4 hours after preparation. Provide enough space so that all pigs can drink the required amount. The actual amount of water consumed may however vary considerably depending on several factors. Therefore, it is recommended

to assess the actual water intake during a 4-hour time period the day before vaccination. Alternatively, refer to the following table:

Body weight (kg)	Water consumption (litres) in a 4-hour time period		
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- For administration using bowls or tanks, dilute the reconstituted vaccine in the volume of water that the pigs will drink during a 4-hour time period.
- For administration through water lines using a dosing pump (proportioner), dilute the reconstituted vaccine in the needed volume of the dosing pump stock solution. The volume of stock solution is calculated using the volume of water that the pigs will drink during a 4-hour time period multiplied by the dosing pump rate (in decimal). As an example, for a 4-hour consumption of 22 litres and a dosing pump rate of 1%, the volume of the stock solution should be 22 litres x 0.01 = 220 ml.

In case of concerns about the presence of disinfectant residues in the drinking water, such as chlorine, it is recommended to add skimmed milk powder as a stabilizer into the drinking water prior to adding the vaccine. The final concentration of the skimmed milk powder should be 5 g/litre.

10. WITHDRAWAL PERIOD(S)

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store and transport refrigerated (2 °C – 8 °C).
Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

Shelf-life after reconstitution and dilution according to directions: 4 hours.

12. SPECIAL WARNING(S)

Special warnings for each target species:

It is not recommended to vaccinate animals undergoing immunosuppressive treatment or to vaccinate animals undergoing antibacterial treatment effective against *E. coli*.

Vaccinate healthy animals only.

Special precautions for use in animals:

The vaccine strains may be excreted by vaccinated piglets for at least 14 days following vaccination. The vaccine strains readily spread to other pigs in contact to vaccinated pigs. Unvaccinated pigs in contact with vaccinated pigs will harbour and shed the vaccine strains similarly to vaccinated pigs. During this time, the contact of immunosuppressed pigs with vaccinated pigs should be avoided.

Special precautions to be taken by the person administering the veterinary medicinal product to animals: Personal protective equipment consisting of protective disposable gloves and safety glasses should be worn when handling the veterinary medicinal product.

In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician. In case of spillage onto skin, rinse with water and seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy:

The use is not recommended during pregnancy.

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), if necessary

A rectal temperature up to 41.2 °C may occur in individual animals within the first 24 hours after administration of a 10-fold overdose.

Incompatibilities:

Do not mix with any other veterinary medicinal product.

13. SPECIAL 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 or pharmacist 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

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

15. OTHER INFORMATION

Pack sizes:

Cardboard box of one vial of 50 or 200 doses.

Cardboard box of four vials of 50 doses.

Not all pack sizes may be marketed.

Immunological properties:

To stimulate active immunity against enterotoxigenic F4-positive and F18-positive *E. coli* in pigs. The vaccine induces an intestinal immunity and a serological response against F4-positive and F18-positive *E. coli* in pigs. The vaccine confers cross protection against F18ab-positive *E. coli*, as demonstrated by challenge for both the 7-day onset of immunity and the 21-day duration of immunity. Antibodies triggered by the vaccine provide cross-reactivity against F4ab and F4ad-positive *E. coli* strains.