SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NUFLOR VETERINARY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Florfenicol 300 mg

Excipients:
N-methyl-2-pyrrolidone 250 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, light yellow to straw-coloured, somewhat viscous solution, Free from foreign matter.

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4. CLINICAL PARTICULARS

4.1 Target species

Cattle and sheep.

4.2 Indications for use, specifying the target species

Treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Haemophilus somnus*.

Treatment of ovine respiratory tract infections due to *Mannheimia haemolytica* and *Pasteurella multocida* susceptible to florfenicol.

4.3 Contraindications

Do not use in adult bulls and rams intended for breeding purposes.
Do not use in the case of known hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

The product should be used in conjunction with susceptibility testing and take into account official and local antimicrobial policies.
The safety of the product has not been established in sheep younger than 7 weeks of age.

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

People with known hypersensitivity to propylene glycol and polyethylene glycols should avoid contact with the veterinary medicinal product. In case of accidental contact with skin or eyes, rinse immediately with plenty of water.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of fetotoxic effects. Women of childbearing age, pregnant women or women suspected of being pregnant should use the veterinary medicinal product with serious caution to avoid accidental self-injection.

4.6 Adverse reactions (frequency and seriousness)

Cattle:
A decrease in food consumption and transient softening of the faeces may occur during the treatment period. The treated animals recover quickly and completely upon termination of treatment.

Intramuscular administration may cause inflammatory lesions at the injection site which may persist for 14 days.

In very rare cases, anaphylactic shock has been reported in cattle.

Sheep:
A decrease in food consumption may occur during the treatment period. The treated animals recover quickly and completely upon termination of treatment.
Intramuscular administration may cause inflammatory lesions at the injection site which may persist up to 28 days. Typically, these are mild and transient.

Reporting suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in cattle and sheep during pregnancy, lactation or in animals intended for breeding. Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of fetotoxic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

No data available.

4.9 Amounts to be administered and administration route

Swab septum before removing each dose. Use a dry sterile needle and syringe.
To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.
The vials should not be broached more than 20 times. User should therefore select the most appropriate vial size according to the target species to be treated.
When treating groups of animals at the same time, use of a draw-off needle in the vial stopper is recommended to avoid excess stopper broaching. The draw-off needle should be removed after treatment.

For treatment
Cattle:
Intramuscular use: 20 mg/kg bodyweight (1 ml/15 kg) to be administered twice 48 hours apart using a 16 gauge needle.
The dose volume given at any one injection site should not exceed 10 ml.
The injection should only be given in the neck.

Sheep:
Intramuscular use: 20 mg florfenicol/kg bodyweight (1 ml/15 kg) to be administered daily for three consecutive days. The volume administered per injection site should not exceed 4 ml.

Pharmacokinetic studies showed that mean plasma concentrations remain above MIC_{90} (1 µg/ml) for up to 18 hours after administration of the product at the recommended treatment dose. The pre-clinical data supported the recommended treatment interval (24 hours) for target pathogens with MIC up to 1 µg/ml.

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

Cattle:
No symptoms other than those described in section 4.6.

Sheep:
After administration of 3 times the recommended dose or more, a transient reduction in feed and water consumption has been observed. Additional effects included an increased incidence of lethargy, emaciation and loose faeces.
Head tilt was seen after administration of 5 times the recommended dose and was considered most likely a result of irritation at the injection site.

4.11 Withdrawal periods

Meat slaughter
Cattle:: 30 days.
Sheep: 39 days.

Milk
Not authorised for use in animals producing milk for human consumption including pregnant animals intended to produce milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for systemic use: Amphenicols.
ATC vet code: QJ01BA90

5.1 Pharmacodynamic properties

Florfenicol is a synthetic broad spectrum antibiotic effective against most Gram-positive and Gram-negative bacteria isolated from domestic animals. Florfenicol acts by inhibiting protein synthesis at the ribosomal level and is bacteriostatic. Laboratory tests have shown that florfenicol is active against the most commonly isolated bacterial pathogens involved in ovine and bovine respiratory disease which include *Mannheimia haemolytica, Pasteurella multocida,* and for cattle *Histophilus somni.*

Florfenicol is considered to be a bacteriostatic agent, but *in vitro* studies of florfenicol demonstrate bactericidal activity against *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni*.

MIC data for the target pathogens are presented in the table below:

Species	**Range (µg/ml)**	**MIC_{50} (µg/ml)**	**MIC_{90} (µg/ml)**
Mannheimia haemolytica (n=151)	0.25 - 2	1	1
Pasteurella multocida (n=88)	0.25 - 0.5	0.5	0.5

Strains were isolated from sheep suffering from respiratory tract infection in Germany, United Kingdom, Spain and France between 2006 and 2010.

5.2 Pharmacokinetic particulars

Cattle:
Intramuscular administration at the recommended dose of 20 mg/kg maintains efficacious blood levels in cattle for 48 hours. Maximum mean serum concentration (C_{max}) of 3.37 µg/ml occurs at 3.3 hours (t_{max}) after dosing. The mean serum concentration 24 hours after dosing was 0.77 µg/ml.

The harmonic mean elimination half-life was 18.3 hours.

Sheep:
After initial intramuscular administration of florfenicol (20 mg/kg), the mean maximum

serum concentration of 10.0 μg/ml is reached after 1 hour. Following the third intramuscular administration, the maximum serum concentration of 11.3 μg/ml is reached after 1.5 hours. The elimination half-life was estimated to be 13.76 + 6.42h. Bioavailability is about 90 %.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

N-methyl-2-pyrrolidone
Propylene glycol
Macrogol

6.2 Incompatibilities

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

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Store below 25 °C.
Do not refrigerate.
Protect from frost.

6.5 Nature and composition of immediate packaging

50, 100 and 250 ml colourless Type I glass vials closed with bromobutyl rubber stoppers with aluminium seals.

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. MANUFACTURER

TriRx Segre
La Grindoliere, Zone Artisanale, Segre
49500 Segre-en-Anjou Bleu, France

8. LICENSE HOLDER

Intervet Israel Ltd.

Industrial Zone Neve Ne'eman 2,
Hod Hasharon 45240,
Israel

9. LICENSE NUMBER
083-32-92230-00

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