CENFLOX 100 mg/ml solution for injection for cattle and pigs

Each ml contains:

Active substance:
Enrofloxacin.....100 mg
Excipients:
n-Butanol .....30 mg
Benzyl alcohol (E1519) .....20 mg

Target species

Cattle and pigs.

Amounts to be administered and administration route

Cattle
The dosage for respiratory disease is 7.5 mg enrofloxacin per kg body weight (bw) for a single treatment by subcutaneous administration (s.c.). This is equivalent to 7.5 ml of the product per 100 kg bw and day.
Do not administer more than 15 ml (cattle) or 7.5 ml (calf) per injection site (subcutaneous).
In case of serious or chronic respiratory disease a second injection may be required after 48 hours.

The dosage for the treatment of colimastitis is 5 mg enrofloxacin per kg body weight (bw) by intravenous administration (i.v.). This is equivalent to 5 ml of the product per 100 kg bw and day.
The treatment of colimastitis should be exclusively by intravenous application on 2 to 3 consecutive days.

Pigs
The dosage for respiratory tract infections is 7.5 mg enrofloxacin per kg body weight for a single administration. This is equivalent to 0.75 ml of the product per 10 kg bw and day.
Do not administer more than 7.5 ml per injection site (intramuscular).
In case of serious or chronic respiratory disease a second injection may be required after 48 hours.

Withdrawal periods

Cattle:
Meat and offal:
s.c. 14 days
i.v.: 7 days
Milk: s.c.: 120 hours (5 days)
i.v.: 72 hours (3 days)

Pig:
Meat and offal: i.m.: 12 days.

Indications for use, specifying the target species

Cattle:
For the treatment of respiratory tract infections caused by enrofloxacin-sensitive *Histophilus somni*, *Mannheimia haemolytica, Pasteurella multocida* and *Mycoplasma* spp.
For the treatment of Mastitis caused by enrofloxacin-sensitive *E.coli*.

Pigs:
For the treatment of bacterial bronchopneumonia caused by enrofloxacin-sensitive *Actinobacillus pleuropneumoniae, Pasteurella multocida* and *Haemophilus parasuis*.

Pharmacodynamic properties

Enrofloxacin belongs to the fluoroquinolone group of antibiotics. The substance has bactericidal activity targeting DNA gyrase and topoisomerase IV with the resulting selective inhibition of these enzymes.
DNA gyrase and topoisomerase IV are the two type II topoisomerases present in bacteria. These enzymes are involved in the replication, transcription and recombination of bacterial DNA. Fluoroquinolones also influence bacteria in the stationary phase by altering cell wall permeability.

The inhibitory and bactericidal concentrations of enrofloxacin are very close, being either identical or differing by no more than 1-2 dilution steps.

Enrofloxacin has a spectrum of activity which includes enrofloxacin-sensitive *Histophilus somni, Mannheimia haemolytica, Pasteurella multocida, Mycoplasma* spp., *E. coli* in cattle as well as *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Haemophilus parasuis* in pigs.

Resistance to fluoroquinolones has been reported to arise from five sources, (i) point mutations in the genes encoding for DNA gyrase and/or topoisomerase IV leading to alterations of the respective enzyme, (ii) alterations of drug permeability in Gram-negative bacteria, (iii) efflux mechanisms, (iv) plasmid mediated resistance and (v) gyrase protecting proteins. All mechanisms lead to a reduced susceptibility of the bacteria to fluoroquinolones. Cross-resistance within the fluoroquinolone class of antimicrobials is common.

MICs values:

Cattle:

MICROORGANISM	ORIGIN	YEAR	Nº STRAINS	MIC 50 (µg/ml)	MIC 90 (µg/ml)
Histophilus somni	Europe	2009-2012 (1)	66	0.03	0.06
Mannheimia haemolytica	Europe	2009-2012 (1)	149	0.03	0.25
Pasteurella multocida	Europe	2009-2012 (1)	134	0.015	0.03
E. coli (mastitis)	Europe	2009-2012 (6)	207	0.03	0.06
Mycoplasma bovis	Europe	2010-2012 (3)	156	0.25	4
	France	2010-2012 (2)	143	0.25	0.5
	Hungary	2010-2013 (4)	35	0.156	0.312
	The Netherlands	2008-2014 (5)	95	0.25	0.5

Pigs:

MICROORGANISM	ORIGIN	YEAR	Nº STRAINS	MIC 50 (µg/ml)	MIC 90 (µg/ml)
Actinobacillus pleuropneumoniae	Europe	2009-2012 (1)	157	0.03	0.06
Pasteurella multocida	Europe	2009-2012 (1)	152	0.015	0.03
Haemophilus parasuis	Europe	2009-2012 (1)	68	0.008	0.06
	Czech Republic	2014-2015 (7)	30	0.03	1

Enrofloxacin resistance breakpoints [R] are available for *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* isolated from cattle (R ≥ 2 µg/ml, CLSI document M31-A3) and for *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* isolated from pigs (R ≥ 1 µg/ml, CLSI document M31-A4).

Pharmacokinetic particulars

Following subcutaneous administration of the product in cattle or intramuscular administration in pigs, the active ingredient, enrofloxacin, is absorbed very rapidly and almost completely (high bioavailability).

Cattle:

After subcutaneous administration at a dose rate of 7.5 mg enrofloxacin per kg body weight to non-lactating cattle peak plasma concentrations of 0.82 mg/L are reached within 5 hours. The overall drug exposure in plasma is 9.1 mg*h/L. Enrofloxacin is eliminated from the body at a half-life of 6.4 h. Approximately 50% of enrofloxacin is metabolized to the active substance ciprofloxacin. Ciprofloxacin is eliminated from the body at a half-life of 6.8 h.

After intravenous injection at a dose rate of 5.0 mg enrofloxacin per kg body weight to lactating cows, peak plasma concentrations of approx. 23 mg/L are reached immediately. The overall drug exposure in plasma is 4.4 mg*h/L. Enrofloxacin is eliminated from the body at a half-life of 0.9 h. Approximately 50% of parent compound are metabolized to ciprofloxacin with peak plasma concentrations of 1.2 mg/L reached at 0.2 h. Elimination half-life is at a mean of 2.1 h.

In milk mainly the metabolite ciprofloxacin accounts for antibacterial activity (approx. 90%). Ciprofloxacin reaches peak milk concentrations of 4 mg/L within 2 hr after intravenous dosing. Total exposure in milk over 24 hours is approx. 21 mg*h/L. Ciprofloxacin is eliminated from milk at a half-life of 2.4 h. Peak concentrations of 1.2 mg enrofloxacin per liter are reached in milk within 0.5 hours with an total enrofloxacin exposure in milk of approx. 2.2 mg*h/L. Enrofloxacin is eliminated from milk at 0.9 h.

Pig:

After intramuscular administration of 7.5 mg/kg body weight to pigs a mean peak serum concentration of 1.46 mg/L was achieved within 4 hours. The overall drug exposure over 24 hours was 20.9 mg*h/L. The drug was eliminated from the central compartment at a terminal half-life of 13.1 h. With peak concentrations less than 0.06 mg/L mean serum concentrations of ciprofloxacin were very low.

Enrofloxacin has a high volume of distribution. The concentrations in the tissues and organs mostly significantly exceed serum levels. Organs in which high concentrations can be expected include the lungs, liver, kidneys, gut and muscle tissue.
Enrofloxacin is eliminated renally.

Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 28 days

Nature and composition of immediate packaging

Amber glass type II vials, with bromobutyl stopper and aluminium cap with FLIP-OFF seal.
Amber polypropylene vials, with bromobutyl stopper and aluminium cap with FLIP-OFF seal.

Pack sizes:

- Box with 1 vial of 100 ml
- Box with 1 vial of 250 ml
- Box with 10 vials of 100 ml
- Box with 10 vials of 250 ml

Not all pack sizes may be marketed.

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