SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

OXTRA DD 100 mg/ml solution for injection for cattle, sheep, pigs, horses, dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Oxytetracycline (as oxytetracycline hydrochloride) 100 mg
Excipients:
Sodium formaldehyde sulfoxylate 5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear yellow to brown-yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, sheep, pigs, horses, dogs and cats.

4.2 Indications for use, specifying the target species

For the treatment of infections caused by organisms susceptible to oxytetracycline in horses, cattle, sheep, pigs, dogs and cats.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in horses during concomitant corticosteroid therapy.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Official and local antimicrobial policies should be taken into account when the product is used.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to oxytetracycline and may decrease the effectiveness of treatment with other tetracyclines due to the potential for cross-resistance.

The product should be used cautiously in animals with hepatic or renal impairment.
Use with caution in horses with gastro-intestinal disturbances or under stress.
See 4.7 before use in male animals.
Do not dilute the product.
If concurrent treatment is administered, use a separate injection site.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This product may cause sensitisation, skin and eye irritation.
People with known hypersensitivity to tetracyclines, such as oxytetracycline, should avoid contact with the veterinary medicinal product.
Avoid contact of the skin and eyes with the product. In case of accidental spillage onto skin or eyes, rinse the affected area with large amounts of water.
Take care to avoid accidental injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Although the product is well tolerated, occasionally a slight local reaction of a transient nature has been observed.
Tetracyclines have also been associated with photosensitivity reactions and, rarely, hepatotoxicity and blood dyscrasias.
Oxytetracycline given to young animals can cause a yellow, brown or grey discolouration of bones and teeth. High dose or chronic administration may delay bone growth or healing.
After intravenous administration of high doses of oxytetracycline in horses, enteritis due to alterations of the intestinal flora can be observed very rarely.
In very rare cases, hypersensitivity (allergic) reactions to treatment may occur, which may require appropriate symptomatic treatment.

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

Laboratory studies have not produced any evidence of embryotoxic or teratogenic effects. However, use only accordingly to the benefit-risk assessment by the responsible veterinarian.

The product can be safely administered to lactating animals.
The active substance, oxytetracycline, readily crosses the placenta and concentrations in the foetal blood may reach those of the maternal circulation, although the concentration is usually somewhat lower. Tetracyclines are deposited in teeth, causing discolouration, enamel hypoplasia and reduced mineralisation. Tetracyclines can also retard foetal skeletal development. As such, the product should only be used in the last half of pregnancy following risk benefit assessment by the responsible veterinarian.
Oxytetracycline is excreted in milk; concentrations are generally low.
Parenteral use of tetracyclines may alter fertility in the male.

4.8 Interaction with other medicinal products and other forms of interaction

Oxytetracycline should not be administered simultaneously with bactericidal antimicrobials, such as penicillins and cephalosporins. Divalent or trivalent cations (Mg, Fe, Al, Ca) can chelate tetracyclines.

4.9 Amounts to be administered and administration route

DD: dual dosage scheme

The product can be administered either every 24 hours at a low dose rate, or at a higher dose rate for prolonged duration of action. To avoid excessive residues at the injection site, maximum injection volumes per injection site are applicable.

Cattle, sheep, pigs, horses: Intramuscular or intravenous use.

Dogs, cats: Subcutaneous or intramuscular use.

To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing.

24 hourly dosage regimen:
Dose rate: 3 – 10 mg/kg body weight depending on age and species (see table).
The treatment may be repeated at 24 hour intervals for 3 to 5 consecutive days.
Intravenous injections must be given slowly over a period of at least one minute.

Prolonged action dosage regimen:
Dose rate: 10 or 20 mg/kg body weight depending on age and species (see table).
Route of administration: Intramuscular injection only, repeated once after 48 – 60 hours if required.
This dosage regimen is not recommended for use in horses, dogs or cats or animals producing milk for human consumption.

Treatment and metaphylaxis of enzootic abortion in sheep:
Dose rate: 20 mg/kg body weight administered between day 95 – 100 of gestation.
A further treatment may be given 2 – 3 weeks later.
For metaphylaxis, the presence of the disease in the group must be established before the product is used.

Clean and disinfect the injection site before administration.
Repeat doses should be administered at different sites, and the sites massaged well after injection.

The maximal volume to be administered per injection site is 20 mL for adult cattle and horses, 10 mL for calves and sheep, and 5 ml for pigs. If larger volumes are required, the injection volumes should be divided over different injection sites.

Animal	Body weight (kg)	24 hourly dose		Prolonged action dose	
		Dose (mg/kg)	Volume (ml)	Dose (mg/kg)	Volume (ml)
Horse	500	5	25	Not recommended	
Foal	100	10	10	Not recommended	
Cow	500	3	15	10	50
Calf	100	8	8	20	20
Sow/boar	150	5	7.5	10	15
Pig	25	8	2	20	5
Sheep	50	8	4	20	10
Lamb	25	8	2	20	5
Dog	10	10	1	Not recommended	
Cat	5	10	0.5	Not recommended	

The 20 ml and 50 ml vials should not be broached more than 40 times; the 100 ml and 250 ml vials should not be broached more than 20 times.
The user should select the most appropriate vial size according to the target species to be treated.

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

Oxytetracycline has a low toxicity, but is an irritant substance. Overdose should be avoided, particularly in horses.
There is no known specific antidote, if signs of possible overdose occur treat the animal symptomatically.

4.11 Withdrawal Period(s)

24-hour dosage regimen

	i.m. use	i.v. use
Cattle:		
Meat and offal	35 days	35 days
Milk	144 hours	144 hours
Sheep:		
Meat and offal	53 days	53 days
Milk	144 hours	144 hours
Pigs:		
Meat and offal	14 days	14 days
Horses:		
Meat and offal	6 month	6 month

Not authorised for use in horses producing milk for human consumption.

Prolonged action dosage regimen

	i.m. use
Cattle:	
Meat and offal	35 days
Sheep:	
Meat and offal	18 days
Pigs:	
Meat and offal	13 days

The prolonged dosage regimen is not authorised for use in animals producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, tetracyclines
ATCvet Code QJ01AA06

5.1 Pharmacodynamic properties

Oxytetracycline is a bacteriostatic antibiotic that inhibits protein synthesis in susceptible bacteria. Inside the cell it binds irreversibly to receptors on the 30S subunit of the bacterial ribosome where it interferes with the binding of the aminoacyl-transfer RNA to the acceptor site on the messenger RNA ribosome complex. This effectively prevents the addition of amino acids to the elongating peptide chain, inhibiting protein synthesis.
Oxytetracycline is a bacteriostatic antibiotic which has broad spectrum antibacterial activity against both Gram-positive and Gram-negative bacteria.
Multiple genes have been identified which mediate resistance to tetracyclines and these genes may be carried on plasmids or transposons between both pathogenic and non-pathogenic bacteria. The most common mechanisms of resistance involve either the removal of the antibiotic from the organism by energy dependent efflux pumps or protection of the ribosome from binding by altered target sites. Resistance to one tetracycline confers cross-resistance across the whole group.

In vitro, oxytetracycline is active against a range of both Gram-positive and Gram-negative microorganisms including: *Streptococcus* spp., *Staphylococcus* spp., *Listeria monocytogenes*, *Mannheimia haemolytica*, *Haemophilus parahaemolyticus* and *Bordetella bronchiseptica*, and against *Chlamydophila abortus*, the causative organism of enzootic abortion in sheep.

The MIC of Oxytetracycline against some of the target bacteria are reported in the following table (source: VetPath 2015-2016, CLSI 2017-2018; ComPath 2013-2014, CLSI 2013-2015):

Species	**Pathogen (number of isolates)**	**MIC 50 *µg/ml***	**MIC 90 *µg/ml***	**Resistance %**

				(CLSI breakpoints *µg/ml*)
Cattle	*Pasteurella multocida* (155)	0.5	8	11.6 (≥8)
	Mannheimia haemolitica (91)	0.5	16	17.6 (≥8)
Horses	*Streptococcus zooepidemicus (164)*	-	-	<74
	Streptococcus equi (26)	-	-	<20
	Actinobacillus equuli (28)	-	-	<14
	Staphilococccus aureus (70)	-	-	<34
Pigs	*Pasteurella multocida* (171)	0.5	2	10.5 (≥2)
	Actinobacilus pleuropneumoniae (164)	0.5	16	21.3 (≥2)
	Streptococcus suis 131)	32	64	82.4 (≥2)
Dogs	*Staphilococccus intermedius* (80)	0.25	>8	45.0 (≥16)
	Staphilococccus aureus (23)	0.5	>8	13.0 (≥16)
	Streptococcus spp (35)	2	>8	40.0 (≥8)
	Bordetella bronchiseptica (25)	1	>8	-
	E. coli (33)	4	>8	18.2 (≥16)
	Pasteurella multocida (14)	0.5	0.5	-
	Pseudomonas aeruginosa (23)	>8	>8	-
Cats	*Streptococcus spp* (23)	4	>8	21.7 (≥8)
	Staphilococccus intermedius (15)	0.25	>8	46.7 (≥16)
	Staphilococccus aureus (16)	0.5	>8	12.5 (≥16)
	CNS (35)	0.5	>8	11.4 (≥16)
	Pasteurella multocida (84)	0.5	0.5	-
	Bordetella bronchiseptica (13)	1	1	-
	Pseudomonas aeruginosa (23)	>8	>8	-
	E. coli (22)	4	>8	13.6 (≥16)

- = not available

5.2 Pharmacokinetic particulars

Oxytetracycline is widely distributed in the body with the exception of CSF and it binds to plasma proteins in a variable manner depending on the species (20-40%). Oxytetracycline is excreted mainly unchanged via the renal route, some in faeces and milk. It is also excreted by the bile but a high proportion of oxytetracycline is reabsorbed by the small intestine (enterohepatic cycle).

5.3 Environmental properties

Oxytetracycline is very persistent in soil.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K12
Ethanolamine
Magnesium oxide light
Sodium formaldehyde sulfoxylate
Hydrochloric acid (10% diluted)
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 the immediate packaging: 28 days.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and composition of immediate packaging

20 ml, 50 ml, 100 ml, 250 ml amber type II glass vials and 100 ml, 250 ml amber PET vials, closed with chlorobutyl rubber stopper type I and sealed with an aluminium collar with a tamper-evident polypropylene seal, in a cardboard box.

Pack-sizes:
1 x 20 ml glass vial
1 x 50 ml glass vial
1 x 100 ml glass or PET vial
1 x 250 ml glass or PET vial
10 x 100 ml glass or PET vial

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Fatro S.p.A.
Via Emilia 285
I-40064 Ozzano Dell'Emilia BO
Italy

8. MARKETING AUTHORISATION NUMBER

Vm 11557/4007

9. DATE OF THE FIRST AUTHORISATION

30 July 2020

10. DATE OF REVISION OF THE TEXT

October 2020

PROHIBITION OF SALE, SUPPLY AND/OR USE

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

Approved 13 November 2020