SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZACTRAN 150 mg/ml solution for injection for cattle, sheep and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Gamithromycin 150 mg

Excipient(s):
Monothioglycerol 1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, sheep and pigs.

4.2 Indications for use, specifying the target species

Cattle:
Treatment and metaphylaxis of bovine respiratory disease (BRD) associated with *Histophilus somni, Mannheimia haemolytica* and *Pasteurella multocida*.
The presence of the disease in the group should be established before the product is used.

Pigs:
Treatment of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae, Bordetella bronchiseptica, Glaesserella parasuis*, and *Pasteurella multocida*.

Sheep:
Treatment of infectious pododermatitis (foot rot) associated with virulent *Dichelobacter nodosus* and *Fusobacterium necrophorum* requiring systemic treatment.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients or to other macrolide antibiotics.
Do not use this veterinary medicinal product simultaneously with other macrolides or lincosamides (see section 4.8).

4.4 Special warnings for each target species

Cattle, pigs and sheep:
Cross resistance has been shown between gamithromycin and other macrolides. Use of the product should be carefully considered when susceptibility testing has shown resistance to other macrolides because its effectiveness may be reduced.
Avoid simultaneous administration of antimicrobials with a similar mode of action such as other macrolides or lincosamides.

Sheep:
The efficacy of antimicrobial treatment of foot rot might be reduced by other factors, such as wet environmental conditions, as well as inappropriate farm management. Treatment of foot rot should therefore be undertaken along with other flock management tools, for example providing dry environment. Antibiotic treatment of benign foot rot is not considered appropriate.

4.5 Special precautions for use

Special precautions for use in animals

Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level. Use of the product should be in accordance with official, national and regional antimicrobial policies.
An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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

People with known hypersensitivity to the macrolide class should avoid contact with the veterinary medicinal product. Gamithromycin may cause irritation to eyes and/or skin.
Avoid contact with skin or eyes. If eye exposure occurs, flush eyes immediately with clean water. If skin exposure occurs, wash the affected area immediately with clean water.
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.

Special precautions for the protection of the environment:
Not applicable.

Other precautions
Not applicable.

4.6 Adverse reactions (frequency and seriousness)

Cattle:

Very common (>1 animal / 10 animals treated)	Injection site swelling[1], injection site pain[2]

[1] Typically resolves within 3 to 14 days but may persist for up to 35 days
[2] Slight pain may develop for 1 day

Sheep:

Common (1 to 10 animals / 100 animals treated)	Injection site swelling[3], injection site pain[4]

[3] Mild to moderate and typically resolves within 4 days
[4] Slight pain may develop for 1 day

Pigs:

Common (1 to 10 animals / 100 animals treated)	Injection site swelling[5]

[5] Mild to moderate and typically resolves within 2 days

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Pregnancy:
Based on laboratory animal data, gamithromycin has not produced any evidence of specific developmental or reproductive 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

See section 4.4.

4.9 Amount(s) to be administered and administration route

A single dose of 6 mg gamithromycin/kg body weight (equivalent to 1 ml/25 kg body weight) into the neck (cattle and pigs) or anterior to the shoulder (sheep).
To ensure correct dose, body weight should be determined as accurately as possible.

Cattle and sheep:
Subcutaneous injection. For treatment of cattle over 250 kg and sheep over 125 kg body weight, divide the dose so that no more than 10 ml (cattle) or 5 ml (sheep) are injected at a single site.

Pigs:
Intramuscular injection. The injection volume should not exceed 5 ml per injection site.

This multi-usage presentation requires an automatic dosing device to be used to avoid excessive broaching of the stopper.

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

Clinical studies have demonstrated the wide margin of safety for gamithromycin injection in the target species. In young adult cattle, sheep and pig studies, gamithromycin was administered by injection at 6, 18, and 30 mg/kg (1, 3, and 5 times the recommended dose) and repeated three times at 0, 5 and 10 days (three times the recommended duration of use). Injection site reactions were noted in a dose related manner.

4.11 Withdrawal period(s)

Meat and offal:
Cattle: 64 days.
Sheep: 29 days.
Pigs: 16 days.

Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 2 months (cows, heifers) or 1 month (ewes) of expected parturition.

5. PHARMACOLOGICAL

Pharmacotherapeutic group: Antibacterials for systemic use, macrolides

ATCvet code: QJ01FA95

5.1 Pharmacodynamic properties

Gamithromycin is an azalide, 15-membered semisynthetic macrolide class antibiotic with uniquely positioned alkylated nitrogen at 7a-position of the lactone ring. This special chemistry facilitates rapid absorption at physiological pH and a long duration of action at the target tissues, the lung and the skin.
Macrolides in general have both bacteriostatic and bactericidal action mediated through disruption of bacterial protein synthesis. Macrolides inhibit bacterial protein biosynthesis by binding to the 50S ribosomal subunit and by preventing peptide chain elongation. The *in vitro* data show that gamithromycin acts in a bactericidal manner. The broad spectrum antimicrobial activity of gamithromycin includes *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni*, *Actinobacillus pleuropneumoniae, Glaesserella parasuis and Bordetella bronchiseptica,* the bacterial pathogens most commonly associated with BRD and SRD, and also *Fusobacterium necrophorum* and *Dichelobacter nodosus*. The MIC and MBC data (cattle and pig) are reported from a representative sample of isolates from field materials within different EU geographic areas.

Cattle	MIC_{90s}	MBC_{90s}
	µg/ml	
Mannheimia haemolytica	0.5	1
Pasteurella multocida	1	2
Histophilus somni	1	2
Pigs	MIC_{90s}	MBC_{90s}
	µg/ml	
Actinobacillus pleuropneumoniae	4	4
Pasteurella multocida	1	2
Glaesserella parasuis	0.5	0.5
Bordetella bronchiseptica	2	4
Sheep	MIC	
	µg/ml	
Fusobacterium necrophorum	MIC_{90}: 32	
Dichelobacter nodosus	0.008 – 0.016	

Three mechanisms are generally considered responsible for resistance to the macrolide class of compounds. This is often referred to as MLS_B resistance as it affects macrolides, lincosamides and streptogramins. The mechanisms involve the alteration of the ribosomal target site, the utilization of active efflux mechanism and the production of inactivating enzymes.

5.2 Pharmacokinetic particulars

Cattle
Gamithromycin administered subcutaneously into the neck of cattle at a single dose of 6 mg/kg body weight, resulted in rapid absorption with peak plasma concentrations observed after 30 to 60 min with a long plasma half-life (> 2 days). The bioavailability of the compound was > 98% with no gender differences.

The volume of distribution at steady-state was 25 l/kg. Gamithromycin levels in lung reached a maximum in less than 24 hr, with lung-to-plasma ratio of > 264 indicating that gamithromycin was absorbed rapidly into the target tissue for BRD.

In vitro plasma protein binding studies determined that the mean concentration of the free active substance was 74%. Biliary excretion of the unchanged drug substance was the major route of elimination.

Pigs
Gamithromycin administered intramuscularly in pigs at single dose of 6 mg/kg body weight, resulted in rapid absorption with peak plasma concentrations observed after 5 to 15 min, with a long plasma half-life (about 4 days). The bioavailability of gamithromycin was > 92%. The compound is absorbed rapidly into the target tissue for SRD. Accumulation of gamithromycin in the lung has been demonstrated by high and sustained concentrations in the lung and bronchial fluid which far exceed those in blood plasma. The volume of distribution at steady-state was approximately 39 l/kg. *In vitro* plasma protein binding studies determined that the mean concentration of the free active drug was 77%. Biliary excretion of the unchanged drug was the major route of elimination.

Sheep
Gamithromycin administered subcutaneously into the neck of sheep at a single dose of 6 mg/kg body weight is rapidly absorbed, and maximum plasma concentrations were observed between 15 minutes and 6 hours after dosing (2.30 hours on average) with high absolute bioavailability of 89%. Gamithromycin skin concentrations were much higher than the plasma concentrations resulting in skin/plasma concentration ratios of approximately 21, 58, and 138 at two, five and ten days post-dosing, respectively, demonstrating extensive distribution and accumulation in skin tissue.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Monothioglycerol
Succinic Acid
Glycerol Formal

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: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Type 1 glass vial of 50, 100, 250 or 500 ml with a chlorobutyl rubber stopper, a polypropylene cap and an aluminium crimp seal or only an aluminium crimp seal.

Polypropylene vial of 100, 250 or 500 ml with a chlorobutyl rubber stopper, a polypropylene cap and an aluminium crimp seal.

Cardboard box containing 1 vial of 50, 100, 250 or 500 ml.

The 500 ml vial is for cattle and pigs only.

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

Medicines should not be disposed of via wastewater.
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

Boehringer Ingelheim Vetmedica GmbH
Binger Strasse 173
55216 Ingelheim am Rhein
Germany

8. MARKETING AUTHORISATION NUMBER

Vm 61700/5082

9. DATE OF FIRST AUTHORISATION

24 July 2008

10. DATE OF REVISION OF THE TEXT

September 2024

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the Product Information Database 'PID' on www.gov.uk.

Approved 04 September 2024
Gavin Hall