1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gamrozyne 150 mg/ml Solution for Injection for Cattle, Sheep and Pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:

Active substance:
Gamithromycin 150 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Monothioglycerol	1 mg
Succinic acid	
Glycerol formal	

Colourless to pale yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle
Sheep
Pigs

3.2 Indications for use for each 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.

3.3 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.

3.4 Special warnings

Cattle, pigs and sheep:

Cross-resistance has been shown between gamithromycin and macrolides or lincosamides. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to macrolides or lincosamides 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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
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.

Not for use for prophylaxis.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product may cause hypersensitivity reactions. 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.

3.6 Adverse events

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 the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of 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.

3.8 Interaction with other medicinal products and other forms of interaction

See section 3.4.

3.9 Administration routes and dosage

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.
The cap may be safely punctured up to 30 times with a 18G needle. In the event of using a 16G needle or for multiple vial entry, an automatic dosing device shall be used to avoid excessive broaching of the stopper.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Cattle:
Meat and offal: 64 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 of expected parturition.

Sheep:
Meat and offal: 29 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 1 month of expected parturition.

Pigs:
Meat and offal: 16 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01FA95

4.2 Pharmacodynamics

Gamithromycin is a semi-synthetic macrolide (CAS No 145435-72-9) prepared by fermentation followed by organic synthesis. The substance is a member of the azalide subclass of macrolide antibiotics consisting of a 15-membered macrocyclic lactone ring.

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, Pasteruella multocida, Histophilus somni, Actinobacillus pleuropneumoniae, Glaesserella parasuis* and *Bordetella bronchiseptica*, *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	

Resistance to macrolides can develop by mutations in genes encoding ribosomal RNA (rRNA) or some ribosomal proteins; by enzymatic modification (methylation) of the 23S rRNA target site, generally giving rise to cross-resistance with lincosamides and group B streptogramins (MLS_B resistance); by enzymatic inactivation; or by macrolide efflux. MLS_B resistance may be constitutive or inducible. Resistance may be chromosomal or plasmid-encoded and may be transferable if associated with transposons, plasmids, integrative and conjugative elements.

4.3 Pharmacokinetics

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 hours, with lung-to-plasma ratio of > 264.
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 volume of distribution at steady-state was approximately 39 L/kg. The compound is absorbed rapidly into the lung. 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.
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 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 27 months.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Store below 30 °C.

5.4 Nature and composition of immediate packaging

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

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

Not all pack sizes may be marketed.

5.5 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 or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Bimeda Animal Health Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA22033/084/001

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).