SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Equigent 100 mg/ml Solution for Injection for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substance

Gentamicin (as gentamicin sulfate)	100 mg

Excipients

Sodium Metabisulphite	1.0 mg
Sodium Methyl parahydroxybenzoate (E219)	0.9 mg
Sodium Propyl parahydroxybenzoate (E217)	0.1 mg

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection.
A clear and colourless to slightly yellow solution, free from particles.

4. CLINICAL PARTICULARS

4.1 Target species

Horses (non-food producing horses).

4.2 Indications for use, specifying the target species

For the treatment of infections of the lower respiratory tract in horses caused by aerobic Gram-negative bacteria susceptible to gentamicin.

4.3 Contraindications

Do not use in known cases of renal dysfunction.
Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.
Do not exceed the proposed dosing regimen.

4.4 Special warnings for each target species

Do not use in horses which are intended to produce meat or milk for human consumption.

4.5 Special precautions for use

Special precautions for use in animals

Gentamicin is well known to induce nephrotoxicity even at therapeutic doses in horses. There are also isolated reports of ototoxicity with gentamicin. No margin of safety has been established under the approved dosing regimen. As such, gentamicin has a narrow margin of safety. The product should therefore only be used based on the benefit-risk assessment by the responsible veterinary surgeon for each individual horse, taking into account alternative available treatment.

In order to reduce the nephrotoxic risk, adequate hydration of animals under treatment should be ensured, and fluid therapy should be instituted, if required.

Close monitoring of horses being treated with gentamicin is strongly advised. This monitoring includes assessing relevant kidney parameters in blood (e.g. creatinine and urea) and urinalysis (e.g. gamma glutamyl transferase/creatinine ratio). Therapeutic blood monitoring of gentamicin concentration is also recommended because of known individual animal variations in peak and trough gentamicin plasma concentrations. Where blood monitoring is available, target peak plasma gentamicin concentrations should be approximately 16–20 µg/ml.

Particular caution should be taken when administering gentamicin with other potential nephrotoxic medicinal products (containing e.g. NSAIDs, furosemide, and other aminoglycosides).

Safety of gentamicin has not been established in foals and there is a lack of knowledge of the extra effects of gentamicin on foal kidneys, especially neonates. Current knowledge suggests that foals, especially neonates, are at a higher risk of gentamicin-induced nephrotoxicity compared to adults.

Differences between neonatal foal kidneys and adults include a slower clearance of gentamicin in foals.

As such, no margin of safety has been established in neonatal foals. It is therefore not recommended to use the product in foals.

Whenever possible, use of the product should be based on susceptibility testing of the bacteria isolated from the animal. Gentamicin is a narrow-spectrum Gram-negative bactericidal antimicrobial, without effects on anaerobe bacteria and mycoplasmas. Gentamicin does not penetrate intracellularly, or into abscesses. Gentamicin is de-activated in the presence of inflammatory debris, low oxygen environments and low pH.

The dosing regimen must not be exceeded. Use of the product deviating from the instructions given in the SPC increases the risk of nephrotoxicity, and may increase the prevalence of bacteria resistant to gentamicin.

Extra caution is advised if using gentamicin in old horses, or with fever, endotoxemia, sepsis and dehydration.

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

Gentamicin may cause hypersensitivity (allergic) reactions following exposure. People with known hypersensitivity to gentamicin should avoid contact with the product. Administer the product with caution.

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

A local reaction may occur at the injection site, especially in case of repeated injections in adjacent sites. See Section 4.5

4.7 Use during pregnancy, lactation or lay

The safety in pregnant horses is unknown. However, studies in laboratory animals have shown evidence of foetal nephrotoxicity. Use only based on the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

This product should not be used in conjunction with other aminoglycoside antibiotics, or with other drugs known to induce either ototoxicity or nephrotoxicity.

4.9 Amounts to be administered and administration route

Administer by slow intravenous injection. Single dose of 6.6 mg gentamicin/kg body weight (equivalent to 0.066 ml/kg b.w. of the product) given intravenously once daily for 3–5 consecutive days.
To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid under- or over-dosing. The dosing regimen must not be exceeded.
The use of gentamicin in foals and neonates is not recommended.

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

The product was not specifically tested in overdose studies and therefore, no margin of safety has been determined.

4.11 Withdrawal period

Not authorised for use in horses producing meat or milk for human consumption

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, gentamicin.
ATCvet code: QJ01GB03.

5.1 Pharmacodynamic properties

Gentamicin sulfate exerts concentration-dependent bacterial killing characteristics. Their rate of killing increases as the gentamicin concentration increases above the minimum concentration (MIC) for a given Gram-negative pathogen, with optimal maximum serum concentration (Cmax) to MIC ratio of 8- 10.
Gentamicin sulfate is bactericidal in action by irreversibly binding to 30S ribosomal subunits, and acts through two different mechanisms. In one mechanism, gentamicin can interfere with the correct amino acid polymerisation and elongation. This mechanism takes place at high concentrations. Another mechanism predominates at low concentrations in which amino acid codons are misread by tRNA and proof-reading is impaired. This leads to incorrect amino acid sequencing and nonsense proteins. The substance is highly polar, hydrophilic and transport appears to be an active process closely linked to electron transport, oxidative phosphorylation and the respiratory quinones in the cell membrane. Gentamicin is best considered as a narrow-spectrum Gram-negative bactericidal antimicrobial (e.g. *E. coli, Proteus* spp*, Pseudomonas* spp). Gentamicin does not have effects on anaerobe bacteria and mycoplasmas. There are several mechanisms by which various strains of bacteria have developed resistance against aminoglycosides like gentamicin. Enzymatic modification is the most common type of aminoglycoside resistance. Over 50 different enzymes have been identified. Enzymatic modification results in high level resistance. The genes encoding for aminoglycoside modifying enzymes are usually found on plasmids and transposons. There are three types of aminoglycoside modifying enzymes:
1. N-Acetyltransferases (AAC) – catalyses acetyl CoA-dependent acetylation of an amino group
2. O-Adenyltransferases (ANT) – catalyses ATP-dependent adenylation of hydroxyl group
3. O-Phosphotransferases (APH) – catalyses ATP-dependent phosphorylation of a hydroxyl group
Two other mechanisms of resistance include ribosomal mutations of the binding site of aminoglycosides, the 30S subunit, and the bacteria decreasing the permeability of aminoglycosides.

Clinical breakpoints for Gentamicin in selected Gram-negative pathogens are as follows:

Bacteria	Susceptible	Intermediate	Resistant	Animal	Source
Enterobacteriaceae	≤ 2	4	≥ 8	Adult horses	CLSI VET08, 2018
Pseudomonas aeruginosa	≤ 2	4	≥ 8	Adult horses	CLSI VET08, 2018
Actinobacillus pleuropneumoniae	≤ 2	4	≥ 8	Adult horses	CLSI VET08, 2018
Acinetobacter spp.	≤ 4	-	≥ 4	Human derived	EUCAST, 2018
Other Gram-negative bacteria relevant for indication	≤ 2	-	≥ 4	Human derived	EUCAST, 2018

5.2 Pharmacokinetic particulars

Gentamicin sulfate is poorly absorbed from the gastrointestinal tract thus the product must be administered parenterally for systemic action. Gentamicin is primarily distributed within extracellular fluids. Gentamicin does not distribute to the cerebrospinal fluid. Gentamicin does not penetrate intracellularly, or into abscesses. Gentamicin is deactivated in the presence of inflammatory debris, low oxygen environments and low pH.
The Vd ranges 0.12 – 0,14 L/kg was detected in adult horses after intravenous administration of 6.6 mg gentamicin/kg b.w. After parenteral administration, gentamicin is distributed to synovial, perilymph, pleural, peritoneal and peri-cardial fluid. Therapeutic concentrations are not achieved in bile, CSF, respiratory secretions and prostatic and ocular fluids. Gentamicin does not cross the placenta of late-term mares. The predominant site of drug accumulation is the renal cortex in most species.
Gentamicin is eliminated unchanged by the kidney via glomerular filtration, including 85–95% of the dose.
The plasma elimination half-lives range from 1 to 3 hours in adult animals but are increased in animals with renal dysfunction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Methyl Hydroxybenzoate (E219)
Sodium Propyl Hydroxybenzoate (E217)
Sodium Metabisulphite
Sodium Citrate (for pH adjustment)
Disodium Edetate
Citric acid monohydrate (for pH adjustment)

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: 30 months
Shelf-life after first opening the immediate packaging: 28 days

6.4 Special precautions for storage

Keep the vial in the outer carton, in order to protect from light.

6.5 Nature and composition of immediate packaging

100 ml and 250 ml clear, Type II glass vial sealed with bromobutyl bung and aluminium overseal.
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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd.
Dublin Road, Loughrea
Co. Galway
Ireland

8. MARKETING AUTHORISATION NUMBER

Vm 08749/4087

9. DATE OF FIRST AUTHORISATION

01 November 2018

10. DATE OF REVISION OF THE TEXT

May 2023

Approved 04 May 2023