PROPOSED PACKAGE INSERT (CLEAN VERSION)

VETERINARY MEDICINE

PROPRIETARY NAME

ZELERIS®

SCHEDULING STATUS

S4

DOSAGE FORM

Solution for Injection

Composition

Each 1 mℓ contains 400 mg florfenicol and 5 mg meloxicam as the active ingredients.

The inactive ingredients are: dimexthyl sulfoxide (DMSO) and glycerol formal (stabilised).

PHARMACOLOGICAL CLASSIFICATION

C17.1.11 Antimicrobial combinations.

INDICATIONS

ZELERIS® is indicated for therapeutic treatment of bovine respiratory disease (BRD) associated with pyrexia due to *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* susceptible to florfenicol.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Florfenicol is a synthetic broad-spectrum antibiotic effective against most Gram-positive and Gram-negative bacteria isolated from domestic animals. Florfenicol acts by inhibiting protein synthesis at the ribosomal level and its action is bateriostatic and time-dependent.

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class which acts by inhibition of prostaglandin synthesis, thereby exerting anti-inflammatory, anti-exudative, analgesic and antipyretic effects. It reduces leukocytes infiltration into the inflamed tissue. Meloxicam also has anti-endotoxic properties; because it has been shown to inhibit production of thromboxane B2 induced by *E. coli* endotoxin after administration in calves, lactating cows and pigs.

Pharmacokinetic properties

After subcutaneous administration of **ZELERIS®** at recommended dose of 1 mℓ / 10 kg bodyweight maximum mean plasma concentration (C_{max}) of 4.6 mg/ℓ and 2.0 mg/ℓ occurred 10 hours and 7 hours after dosing for florfenicol and meloxicam respectively.

Florfenicol is largely distributed in the whole body and has a low plasma protein binding (approximately 20%). Meloxicam is extensively bound to plasma proteins (97%) and is distributed in all well-perfused organs.

Florfenicol is mainly excreted via the urine and to a small extent via the faeces with a half-life of about 60 hours. Meloxicam excretion is equally divided between urine and

faeces, with half-life of about 23 hours.

CONTRA-INDICATIONS

Do not use in adult bulls intended for breeding.

Do not use in animals suffering from impaired hepatic, cardiac or renal function and haemorrhagic disorders or when there is evidence of ulcerogenic gastrointestinal lesions.

Do not use in case of hypersensitivity to the active substances or to any of the excipients.

WARNINGS OR WITHDRAWAL PERIOD

Withdrawal period:

Meat and offal: Do not slaughter animals for human consumption within 56 days after the last subcutaneous treatment.

Milk: Not authorised for use in lactating animals producing milk for human consumption. Do not use in pregnant cows which are intended to produce milk for human consumption within two months of expected parturition.

In the absence of compatibility studies, **ZELERIS®** must not be mixed with other veterinary medicinal products.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Injection site reaction such as swelling, induration, heat and pain were commonly observed after subcutaneous administration of the product. These effects were transitory and usually resolved without any treatment within 5 to 15 days, but could persist up to 49 days. During injection of this product animals may exhibit signs of moderate pain, manifested as movement of the head or neck.

Special precautions for use in animals

Whenever possible, **ZELERIS®** should only be used based on susceptibility testing.

Avoid use in severely dehydrated, hypovolaemic or hypotensive animals, as there may be a potential risk of renal toxicity.

In the absence of safety data, it is not recommended to use the product in calves less than 4 weeks old.

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

The product is slight irritant to the eye. Rinse any splashes from eyes immediately with plenty of water.

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

People with known hypersensitivity to florfenicol, meloxicam or to any excipients should avoid contact with this veterinary medicinal product.

Dose dependent maternotoxic and foetotoxic effects have been observed after oral administration of meloxicam to pregnant rats; therefore **ZELERIS®** should not be administered by pregnant women.

KNOWN SIGNS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

The administration of three or five times the recommended dose weekly in calves was associated with decreased milk consumption, decreased weight gain, loose faeces or diarrhoea. Repeated weekly administration of three times dose was fatal in 1 out of 8 calves after the third administration. Repeated weekly administration of five times dose was fatal in 7 out of 8 calves after the third administration. Extent of these adverse effects was dose-dependent.

QUANTITY AND STRENGTH OF ACTIVE INGREDIENTS PER DOSAGE UNIT

Subcutaneous use.

A single subcutaneous injection of **ZELERIS®**, at a dosage of 40 mg florfenicol/kg bodyweight and 0.5 mg meloxicam/kg bodyweight (i.e.: 1 mℓ / 10 kg bodyweight).

The single dose volume should not exceed 15 mℓ per injection site.

The injection should only be given in the neck area.

To ensure correct dosage, bodyweight should be determined as accurately as possible to avoid under dosing.

For 250 mℓ vials, the rubber stopper may safely be punctured up to 20 times.

The use of multi-dose syringe is recommended.

INTERACTIONS

Do not administer concurrently with glucocorticoids other non-steroidal anti-inflammatory drugs or with anticoagulant agents.

STORAGE INSTRUCTIONS

Store at or below 25 ˚C.

Keep out of reach of children and uninformed persons.

Shelf-life of opened bottle: 28 days.

IDENTIFICATION

Clear yellow solution.

PRESENTATION:

ZELERIS® is available in three commercial presentations:

- 50 mℓ translucent multi-layer plastic vials

- 100 mℓ translucent multi-layer plastic vials

- 250 mℓ translucent multi-layer plastic vials

The 50 mℓ and 100 mℓ vials are closed with 20 mm diameter chlorobutyl stoppers.

The 250 mℓ are closed with 32 mm diameter chlorobutyl stoppers.

REGISTRATION NUMBER:

C17/17.1.11/19 (Act 101/1965)

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Ceva Animal Health (Pty) Ltd

P O Box 7707,

Halfway House, Midrand,

South Africa,

1685

Tel: 087 310 9728

Fax: 011 312 4092

Website: www.ceva.co.za

DATE OF NOTIFICATION OF APPROVAL OF THIS SCIENTIFIC PACKAGE INSERT

17 November 2020