1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Histodine 10 mg/ml solution for injection for cattle (BE, CY, CZ, EE, ES, HU, IE, IS, IT, LT, LU, LV, NL, PL, PT, RO, SK, UK)
Histodine solution for injection for cattle (FR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substance:
Chlorphenamine maleate 10 mg
(equivalent to 7.03 mg chlorphenamine)

Excipients:
Methyl parahydroxybenzoate (E218) 1.0 mg
Propyl parahydroxybenzoate 0.2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

For the symptomatic treatment of conditions associated with histamine release.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Do not administer via subcutaneous route.

Although intravenous administration has an immediate therapeutic effect, it can have excitatory effects on the CNS. Consequently, administer slowly and interrupt administration for a few minutes if necessary, when using this route.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Chlorphenamine can cause sedation. Wash splashes from skin and eyes immediately. Precautions should be taken to avoid accidental self-injection with this drug. Preferably use a guarded needle until the moment of injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. DO NOT DRIVE.

4.6 Adverse reactions (frequency and seriousness)

Chlorphenamine has a weak sedative effect.

4.7 Use during pregnancy and lactation

The safety of the product has not been established during pregnancy and lactation. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

Concomitant use of other antihistamines or barbiturates may boost the sedative effect of chlorphenamine. The use of antihistamines may conceal early signs of ototoxicity caused by some antibiotics (i.e. aminoglycosides and macrolides) and may shorten the effect of oral anticoagulants.

4.9 Amounts to be administered and administration route

Intramuscular or intravenous use.
Intravenous injection should be slow and, if necessary, discontinued for a few minutes (see 4.5).

Adult animals:
0.5 mg Chlorphenamine maleate /kg bodyweight (equivalent to 5 ml/100 kg bodyweight), once a day for three consecutive days.

Calves:
1 mg Chlorphenamine maleate /kg bodyweight (equivalent to 10 ml/100 kg bodyweight), once a day for three consecutive days.

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

Doses up to four times the therapeutic dose have been well tolerated. In very rare cases, local reactions were observed at the injection site. All the reactions were transient and resolved spontaneously.

4.11 Withdrawal periods

Meat and offal: 1 day
Milk: 12 hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antihistamines for systemic use.
ATC vet code: QR06AB04

5.1 Pharmacodynamic properties

Chlorphenamine maleate is a racemic compound classified as an alkyl amine group antihistamine that, due to its chemical characteristics, is able to bind to the H1 receptor present on the cell membrane and therefore compete with the natural endogenous ligand for the same site. Receptor occupation by chlorphenamine maleate does not, in itself, induce pharmacological responses, but significantly inhibits those induced by histamine. On the basis of these observations, chlorphenamine maleate behaves as a direct or reversible competitive receptor antagonist. Chlorphenamine maleate is not able to inhibit the synthesis or release of histamine.

5.2 Pharmacokinetic particulars

After intravenous administration the medicinal product's plasma concentration drops from 36 ng/mL to the method's limit of detection (1 ng/mL) 24 hours after administration. The calculated elimination half-life ($T_{1/2ß}$) is 2.11 hours, the mean residence time (MRT) is 2.35 hours, total clearance (Cl_B) 1.315 L/kg/h and the volume of distribution (Vd) just over 3 L/kg. Following intramuscular administration, peak concentration (C_{max} = 142 ng/mL) is reached in 28 minutes (T_{max}). Plasma concentrations then drop rapidly to reach values of 60 and 12 µg/kg after 2 and 8 hours before dropping below the limit of quantification (1 µg/kg) 24 hours after treatment. MRT and bioavailability were 3.58 hours and 100%, respectively.
The compound and its metabolites are excreted primarily via the kidneys in urine, with a small amount in unmodified form and the majority as a breakdown product, almost completely, within 24 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Disodium phosphate dodecahydrate
Sodium dihydrogen phosphate dihydrate
Water for injection

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after opening of the immediate packaging: 56 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage precautions.
Store in the original package in order to protect from light.

6.5 Nature and composition of the immediate packaging

Clear Type II glass vials and polypropylene vials containing 100 ml or 250 ml, closed with a coated

bromobutyl rubber stopper and aluminium cap in a carton box.
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

Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of first authorisation:
Date of last renewal:

10. DATE OF REVISION OF THE TEXT

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PROHIBITION OF SALE, SUPPLY AND / OR USE