

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Mastavance 20 mg intramammary suspension for cattle (lactating cow)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each syringe (8.7 g) contains:

Active substances:

Hydrocortisone aceponate..... 20 mg

Excipients:

Qualitative composition of excipients and other constituents
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Paraffin light liquid

Vaseline codex T5*

*vaseline codex T5 is a ready-to-use mixture composed of Paraffin liquid, microcrystalline wax and Paraffin hard.

White to yellowish oily suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (lactating cow).

3.2 Indications for use for each target species

For the symptomatic treatment of mild to moderate clinical mastitis affecting a single udder quarter. The veterinary medicinal product can be used to treat inflammation, pain and discomfort when first signs of clinical mastitis are observed, pending confirmation of the pathogen involved (if present) and decision to administer further treatment if needed.

3.3 Contraindications

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

3.4 Special warnings

The veterinary medicinal product is intended to be used in mild and moderate cases of clinical mastitis in a single udder quarter, showing visible abnormalities in the milk (presence of clots or flakes) and/or in the udder (swelling of the quarter, heat on the skin surface, erythema, pain at palpation) with the absence of severe local signs or systemic signs of illness such as pyrexia, anorexia or recumbency.

The veterinary medicinal product has not been tested in animals with a known history of subclinical mastitis, with mastitis relapsing in the same quarter in the month preceding the treatment, with a damaged teat.

Efficacy has not been investigated with other milking routines than 12-hour intervals.

It is recommended to take a milk sample for bacteriological culture and antimicrobial susceptibility testing before the first administration and to use the veterinary medicinal product whilst waiting on the

milk analysis results.

Based on clinical response to the treatment and/or milk analysis results, a follow-on course of another appropriate treatment might be used as needed.

Post-treatment relapse or any persistence, worsening of symptoms require immediate reassessment.

Therefore, close monitoring of cows should be considered.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Not applicable.

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

Veterinary medicinal product: The active substance of this veterinary medicinal product, hydrocortisone aceponate, is potentially pharmacologically active and may be harmful to the unborn child at high doses of exposure.

Avoid skin contact and ingestion, including hand-to-mouth contact, especially pregnant women.

In case of accidental skin contact, wash the exposed area immediately with water.

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

Wash hands after use.

Cleaning towel: The cleaning towels provided with the intramammary product contain isopropyl alcohol which is an eye irritant and may cause skin irritation.

Avoid skin and eye contact, including hand-to-eye contact.

In case of accidental skin or eye contact, rinse skin or eye immediately with plenty of water. If irritation persists, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

The cleaning towel is flammable. Do not use close to an open flame or any other incandescent material. Do not smoke when handling the cleaning towel.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle (lactating cow)

Very common (>1 animal / 10 animals treated):	Neutrophilia ¹ , Hypocortisolaemia ^{1,2} , Monocytosis ¹ , Hyperglycaemia ¹ , Eosinopenia ¹ ,
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¹ Spontaneously reversible within 6 days post-treatment end, and not associated with clinical signs.

² Only observed after adrenocorticotrophic hormone (ACTH) stimulation test.

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

3.7 Use during pregnancy, lactation or lay

Pregnancy

Can be used during pregnancy.

Lactation:

Glucocorticoids are excreted in the milk and may result in growth impairment in suckling young animals.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Intramammary use.

After complete milking and before administering the veterinary medicinal product, the teats should be thoroughly cleaned and disinfected using a cleaning towel, and care should be taken to avoid contamination of the syringe nozzle. Insert the syringe cannula only partially to prevent pushing bacteria-contaminated keratin into the teat cistern and reduce sphincter dilatation.

Administer the full content of one syringe through the teat canal into the affected quarter by pressing the plunger. After treatment, apply a teat dip ensuring complete coverage.

If clinical cure is not achieved after a single application, other administration(s) may be required every 12 hours up to maximum 3 additional doses per quarter. Massage after administration. Do not milk immediately after treatment.

A clinical cure should be observed within 6 days after the start of treatment. In case of worsening or in case the mastitis is not cured, or in case of recurrence of clinical mastitis in the same quarter within a month, immediate reassessment is required and the use of another treatment should be considered.

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

In an overdose study in dairy cattle up to 4X the recommended dosage (i.e., application of the veterinary medicinal product in all 4 quarters of the udder) with an extended treatment duration (3X the maximum recommended treatment duration), administration of the veterinary medicinal product was associated with changes on some blood haematology and biochemistry parameters, reduction of the capacity of production of cortisol, and decreased milk production or composition change. All these pharmacological effects were of low magnitude, non-adverse, and rapidly reversible.

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

Meat and offal: Zero days.

Milk: 24 hours.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QG52X

4.2 Pharmacodynamics

The veterinary medicinal product contains the active substance hydrocortisone aceponate. Hydrocortisone aceponate (HCA) belongs to the diester class of the glucocorticosteroids with a potent intrinsic local glucocorticoid activity. Hydrocortisone aceponate is metabolized in the epithelium by esterases into different metabolites including a 17-monoester which also has an anti-inflammatory effect. The veterinary medicinal product reduces udder inflammation (redness and swelling), pain and discomfort associated with mild to moderate clinical mastitis.

4.3 Pharmacokinetics

After intramammary administration of the veterinary medicinal product (one syringe [20 mg] every 12 hours for 4 administrations), no plasma availability and systemic exposure of hydrocortisone aceponate was observed (hydrocortisone aceponate < LLOQ 0.2 ng/mL). Hydrocortisone aceponate is metabolised to physiologically active corticosteroid compounds related to physiological cortisol. The absorbed physiologically active corticosteroid compounds cause a transient decrease of systemic cortisol plasma concentrations for up to 12 hours after treatment. These corticosteroid compounds are expected to follow the same hepatic metabolic pathway as endogenous cortisol with some renal excretion.

Hydrocortisone aceponate was quantifiable in milk from the treated quarter up to 24 hours after the last administration (T_{max} 2.5 hours after the last administration; C_{max} 9 550 $\mu\text{g}/\text{kg}$; elimination $t_{1/2}$ 2 hours). Hydrocortisone aceponate was below the limit of quantification (<0.2 ng/ml) in milk from the untreated quarters.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

White to yellowish opaque pre-filled intramammary syringe made of Low-density Polyethylene (LDPE) closed with LDPE nozzle cap or dual cap.

Pack sizes:

Cardboard box containing 12 intramammary syringes and 12 cleaning towels.

Cardboard box containing 24 intramammary syringes and 24 cleaning towels.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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

Virbac

7. MARKETING AUTHORISATION NUMBER(S)

VPA10988/120/001

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>).