[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zitac vet 200 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Cimetidine 200 mg per tablet

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate
Cellulose, microcrystalline
Maize starch pregelatinised
Sodium starch glycolate (type A)
Magnesium stearate

White, oblong tablets, scored on both sides.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Symptomatic treatment for the reduction of vomiting associated with chronic gastritis in dogs.

3.3 Contraindications

None.

3.4 Special warnings

Treatment with cimetidine is symptomatic only and does not result in resolution of histopathological changes associated with gastritis. It is recommended that dogs showing persistent vomiting should undergo appropriate investigations to diagnose the underlying cause before starting treatment. This is especially important in older animals. The reduction of gastric acidity caused by cimetidine may contribute to bacterial overgrowth and antigenic stimulation.

3.5 Special precautions for use

Special precautions for safe use in the target species:

In case of renal dysfunction, adjustment of the dose may be required as the clearance of cimetidine may be decreased. If the response to treatment is poor within 15 days, the diagnosis and treatment plan should be re-evaluated.

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

None.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Mammary gland swelling[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Prostate weight reduction[2]

[1] Transient and self-resolving, slight swelling (gynaecomastia); anti-androgenic activity.
[2] reversible, with no impact on reproductive performances

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 and lactation:

The use of the veterinary medicinal product during pregnancy and lactation in the target species has not been investigated. Therefore, use of the veterinary medicinal product during pregnancy and lactation should be based on a risk benefit-assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Due to inhibition of cytochrome P-450 activity by cimetidine, the metabolism and elimination of some drugs can be reduced. Clinically relevant interactions may occur with compounds having a narrow therapeutic index, e.g. beta-blockers, calcium channel blockers, benzodiazepines, barbiturates, phenytoin, theophylline, aminophylline, warfarin and lidocaine. Doses of such drugs may need to be reduced when administered concomitantly with cimetidine.

The increased gastric pH resulting from cimetidine administration may lead to reduced absorption of drugs requiring an acid medium for absorption. It is recommended that at least 2 hours should elapse between administration of cimetidine and aluminium or magnesium hydroxide, metoclopramide, digoxin or ketoconazole when possible.

3.9 Administration routes and dosage

For oral use.
Dose and route of administration: 5 mg of cimetidine per kg of bodyweight administered three times daily by the oral route (see indicative table below). The concomitant use of appropriate dietary measures is strongly recommended. In clinical trials the efficacy of cimetidine has only been studied concomitantly with a hypoallergenic diet.

Table: Number of Zitac vet 200 mg tablets to be administered three times daily according to body weight.

Weight (kg)	Number of Zitac vet 200 mg tablets
11 to 20	½
21 to 40	1
41 to 60	1 ½

Recommended treatment scheme: reduction of vomiting is achieved in about 2 weeks. Animals should however be treated for at least 2 weeks after the remission of clinical signs, so a minimum treatment duration of 28 days is usually necessary and therefore recommended. If considered successful, medication should be withdrawn for 2 weeks. If vomiting occurs again, treatment can be re-initiated without risk of intolerance.

Depending on the response, treatment can be adapted to the individual animal until the response is considered to be adequate and continued. Dietary measures should always be maintained.

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

Acute exposure to cimetidine yielded LD_{50} values above 2600 mg/kg, *i.e.* over 170 times the recommended daily dosage in dogs. A target animal safety study in dogs demonstrated that the veterinary medicinal product administered orally at 75 mg cimetidine/kg/day (five times the recommended daily dose) for a period of 91 days was well tolerated by dogs.
No signs of overdose are known.

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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QA02BA01.

4.2 Pharmacodynamics

Cimetidine is an antagonist of the histamine H2-receptors present in the gastric parietal cells. Stimulation of H2-receptors by histamine activates gastric acid secretion. Cimetidine, via its antagonistic properties toward histamine H2-receptors, strongly reduces gastric acid secretion. This may result in the diminution of gastric irritation and subsequent vomiting during chronic gastritis. No accompanying improvement in the inflammatory status of the gastric mucosa was observed in dogs.

4.3 Pharmacokinetics

After oral administration of the veterinary medicinal product at a dose rate of 5 mg/kg body weight to fasted dogs, maximal plasma levels of approximately 2 µg/ml are reached after 1.5 hours post-

administration. Bioavailability is about 95%. The extent of absorption of cimetidine in dogs is delayed and reduced by approximately 40 % in the presence of food ($C_{max\ fasted}$ 2.94 mcg/ml, $C_{max\ fed}$ 1.12 mcg/ml, $AUC_{0-\infty\ fasted}$ 8.23 mcg.h/ml and $AUC_{0-\infty\ fed}$ 5.43 mcg.h/ml). However, this does not affect the efficacy of treatment.

The plasma half-life of cimetidine is approximately 2 hours at a dosage of 5 mg/kg. Cimetidine is rapidly and almost completely excreted into the urine. No drug accumulation occurs after repeated oral treatment at 5 mg/kg three times daily over 30 consecutive days.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

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

5.3 Special precautions for storage

Store the blisters in the original package to protect from light. Remaining tablet halves should be stored in the original blister pocket in order to protect from light.

5.4 Nature and composition of immediate packaging

The tablets are packed in push-through blisters (white opaque PVC/Aluminium foil) in an outer printed carton box.

Authorised pack sizes:
Carton box containing 30 tablets (3 blister with 10 tablets per blister)
Carton box containing 100 tablets (10 blister with 10 tablets per blister)

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

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:{DD/MM/YYYY}

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

{DD/MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
NL: Veterinary medicinal product not subject to prescription.

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

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton Box Zitac vet 200 mg tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zitac vet 200 mg tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Cimetidine 200 mg per tablet.

3. PACKAGE SIZE

30 tablets
100 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

NL: <Symptomatic treatment for the reduction of vomiting associated with chronic gastritis in dogs.>

6. ROUTES OF ADMINISTRATION

For oral use, 5 mg/kg bodyweight three times daily.

7. WITHDRAWAL PERIODS

Withdrawal period:
Not applicable.

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store the blisters in the original package to protect from light. Remaining tablet halves should be stored in the original blister pocket in order to protect from light.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister Zitac vet 200 mg tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zitac vet 200 mg tablets

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Cimetidine 200 mg per tablet.

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Zitac vet 200 mg tablets for dogs.

2. Composition

Active substance:

Cimetidine 200 mg per tablet

White, oblong tablets, scored on both sides.

3. Target species

Dogs.

4. Indications for use

Symptomatic treatment for the reduction of vomiting associated with chronic gastritis in dogs.

5. Contraindications

None.

6. Special warnings

Special warnings:

Treatment with cimetidine is symptomatic only and does not result in resolution of histopathological changes associated with gastritis. It is recommended that dogs showing persistent vomiting should undergo appropriate investigations to diagnose the underlying cause before starting treatment. This is especially important in older animals. The reduction of gastric acidity caused by cimetidine may contribute to bacterial overgrowth and antigenic stimulation.

Special precautions for safe use in the target species:

In case of renal dysfunction, adjustment of the dose may be required as the clearance of cimetidine may be decreased. If the response to treatment is poor within 15 days, the diagnosis and treatment plan should be re-evaluated.

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

None.

Pregnancy and lactation:

The use of the veterinary medicinal product during pregnancy and lactation in the target species has not been investigated. Therefore, use of the veterinary medicinal product during pregnancy and lactation should be based on a risk-benefit-assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

Due to inhibition of cytochrome P-450 activity by cimetidine, the metabolism and elimination of some drugs can be reduced. Clinically relevant interactions may occur with compounds having a narrow therapeutic index, e.g. beta-blockers, calcium channel blockers, benzodiazepines, barbiturates, phenytoin, theophylline, aminophylline, warfarin and lidocaine. Doses of such drugs may need to be reduced when administered concomitantly with cimetidine.

The increased gastric pH resulting from cimetidine administration may lead to reduced absorption of drugs requiring an acid medium for absorption. It is recommended that at least 2 hours should elapse between administration of cimetidine and aluminium or magnesium hydroxide, metoclopramide, digoxin or ketoconazole when possible.

Overdose:

No signs of overdose are known.

7. Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Mammary gland swelling[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Prostate weight reduction[2]

[1] Transient and self-resolving, slight swelling (gynaecomastia); anti-androgenic activity.
[2] reversible, with no impact on reproductive performances

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or the local representative of the marketing authorisation holder> using the contact details at the end of this leaflet, or via your national reporting system: <{national system details}

8. Dosage for each species, routes and method of administration

For oral use.
Dose and route of administration: 5 mg of cimetidine per kg of bodyweight administered three times daily by the oral route. The concomitant use of appropriate dietary measures is strongly recommended. In clinical trials the efficacy of cimetidine has only been studied concomitantly with a hypoallergenic diet.

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Depending on the response, treatment can be adapted to the individual animal until the response is considered to be adequate and continued. Dietary measures should always be maintained.

9. Advice on correct administration

None.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store the blisters in the original package to protect from light. Remaining tablet halves should be stored in the original blister pocket in order to protect from light.
Do not use after expiry date which is stated on the carton.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your <veterinary surgeon> <or> <pharmacist> how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.
NL: Veterinary medicinal product not subject to prescription.

14. Marketing authorisation numbers and pack sizes

{< > MA no. to be adjusted nationally}

Carton box containing 30 tablets (3 blister with 10 tablets per blister)
Carton box containing 100 tablets (10 blister with 10 tablets per blister)
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>

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

16. Contact details

Marketing authorisation holder <and contact details to report suspected adverse reactions>:
{<>to be adjusted nationally}

Manufacturer responsible for batch release:
Intervet GesmbH
Siemensstrasse 107
1210 Vienna
Austria

<Local representatives <and contact details to report suspected adverse reactions>:>
{<>to be adjusted nationally}

<For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.
{<>to be adjusted nationally}