SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Arocenia 10 mg/ml solution for injection for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
10 mg of maropitant as maropitant citrate monohydrate

Excipients:
Benzyl alcohol E1519 11.1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Clear, colourless to light yellow or to slightly brown solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats.

4.2 Indications for use, specifying the target species

Dogs
- For the treatment and prevention of nausea induced by chemotherapy.
- For the prevention of vomiting except that induced by motion sickness.
- For the treatment of vomiting, in combination with other supportive measures.
- For the prevention of perioperative nausea and vomiting and improvement in recovery from general anaesthesia after use of the μ-opiate receptor agonist morphine.

Cats
- For the prevention of vomiting and the reduction of nausea, except that induced by motion sickness.
- For the treatment of vomiting, in combination with other supportive measures.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Vomiting can be associated with serious, severely debilitating conditions including gastrointestinal obstructions; therefore, appropriate diagnostic evaluations should be employed.

Good veterinary practice indicates that antiemetics should be used in conjunction with other veterinary and supportive measures such as dietary control and fluid replacement therapy while addressing the underlying causes of the vomiting.

The use of the veterinary medicinal product against vomiting due to motion sickness is not recommended.

Dogs:
Although maropitant has been demonstrated to be effective in both the treatment and prevention of emesis induced by chemotherapy, it was found more efficacious if used preventively. Therefore, it is recommended to administer the antiemetic prior to administration of the chemotherapeutic agent.

Cats:
The efficacy of maropitant in reduction of nausea was demonstrated in studies using a model (xylazine induced nausea).

4.5 Special precautions for use

i) Special precautions for use in animals:

The safety of the veterinary medicinal product has not been established in dogs less than 8 weeks of age, or in cats less than 16 weeks of age, and in pregnant or lactating dogs and cats. Use only according to the benefit-risk assessment by the responsible veterinarian.

Maropitant is metabolised in the liver and therefore should be used with caution in patients with hepatic disease. As maropitant is accumulated in the body during a 14-day treatment period due to metabolic saturation, careful monitoring of liver function and any adverse events should be implemented during long term treatment.

The veterinary medicinal product should be used with caution in animals suffering from or with predisposition for cardiac diseases as maropitant has affinity to Ca- and K-ion channels. Increases of approximately 10% in the QT interval of the ECG were observed in a study on healthy beagle dogs administered 8 mg/kg orally; however, such an increase is unlikely to be of clinical significance.

Due to the frequent occurrence of transient pain during subcutaneous injection, appropriate animal restraining measures may have to be applied. Injecting the veterinary medicinal product at refrigerated temperature may reduce pain at injection.

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

Maropitant is a neurokinin-1 (NK1) receptor antagonist that acts in the central nervous system. The veterinary medicinal product may therefore cause nausea, dizziness and drowsiness in case of accidental self-injection. If accidental self-injection occurs, seek medical advice immediately and show the package leaflet or the label to the physician.
Due to the content of benzyl alcohol the veterinary medicinal product may cause mild local irritation. Skin contact should therefore be avoided. In case of accidental exposure, wash affected skin area with plenty of water.
The veterinary medicinal product may cause skin sensitisation. People with known hypersensitivity to maropitant or to any of the excipients should administer the veterinary medicinal product with caution. If you develop symptoms such as a skin rash after accidental exposure, seek medical advice and show the physician this warning.
The veterinary medicinal product may cause eye irritation. Eye contact should be avoided. In case of accidental eye exposure, flush the eyes with plenty of water and seek medical attention.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Dogs, cats:

Very common (>1 animal / 10 animals treated):	Injection site pain.[1,2]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic-type reaction (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membrane). Lethargy. Neurological disorders (ataxia, convulsion/seizure or muscle tremor).

[1]When injected subcutaneously to cat: moderate to severe response to injection (in approximately one third of cats).
[2]When injected subcutaneously to dog.

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 contact details.

4.7 Use during pregnancy, lactation or lay

Use only according to the benefit-risk assessment by the responsible veterinarian, because conclusive reproductive toxicity studies have not been conducted in any animal species.

4.8 Interaction with other medicinal products and other forms of interaction

The veterinary medicinal product should not be used concomitantly with Ca-channel antagonists as maropitant has affinity to Ca-channels.

Maropitant is highly bound to plasma proteins and may compete with other highly bound medicines.

4.9 Amount(s) to be administered and administration route

For subcutaneous or intravenous use in dogs and cats.

The veterinary medicinal product should be injected subcutaneously or intravenously, once daily, at a dose of 1 mg/kg bodyweight (1 ml/10 kg bodyweight) for up to 5 consecutive days. Intravenous administration of the veterinary medicinal product should be given as a single bolus without mixing the veterinary medicinal product with any other fluids.

To prevent vomiting, the veterinary medicinal product should be administered more than 1 hour in advance. The effect duration is approximately 24 h and therefore treatment can be given the night before administration of an agent that may cause emesis e.g. chemotherapy.

As the pharmacokinetic variation is large and maropitant accumulates in the body after once daily repeated administration, lower doses than recommended might be sufficient in some individuals and when repeating the dose.

For administration by subcutaneous injection, see also “Special precautions for use in animals:” (section 4.5).

The cap may be safely punctured up to 40 times. It is recommended that a draw-off needle be used to reduce the number of times the septum is punctured.

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

Apart from transient reactions at the injection site following subcutaneous administration, maropitant was well tolerated in dogs and young cats injected daily with up to 5 mg/kg (5 times the recommended dose) for 15 consecutive days (3-times the recommended duration of administration). No data have been presented on overdoses in adult cats.

4.11 Withdrawal periods

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiemetics
ATCvet code: QA04AD90.

5.1 Pharmacodynamic properties

Vomiting is a complex process coordinated centrally by the emetic centre. This centre consists of several brainstem nuclei (area postrema, nucleus tractus solitarius, dorsal motor nucleus of the vagus) that receive and integrate sensory stimuli from central and peripheral sources and chemical stimuli from the circulation and the cerebro-spinal fluid.

Maropitant is a neurokinin 1 (NK_1) receptor antagonist, which acts by inhibiting the binding of substance P, a neuropeptide of the tachykinin family. Substance P is found in significant concentrations in the nuclei comprising the emetic centre and is considered the key neurotransmitter involved in vomiting. By inhibiting the binding of substance P within the emetic centre, maropitant is effective against neural and humoral (central and peripheral) causes of vomiting.

A variety of *in vitro* assays have demonstrated that maropitant binds selectively at the NK_1 receptor with dose-dependent functional antagonism of substance P activity.

Maropitant is effective against vomiting. The anti-emetic efficacy of maropitant against central and peripheral emetics was demonstrated in experimental studies including apomorphine, cisplatin and syrup of ipecac (dogs) and xylazine (cats). Signs of nausea in dogs including excessive salivation and lethargy might remain after treatment.

5.2 Pharmacokinetic properties

Dogs
The pharmacokinetic profile of maropitant when administered as a single subcutaneous dose of 1 mg/kg body weight to dogs was characterised by a maximum concentration (C_{max}) in plasma of approximately 92 ng/ml; this was achieved within 0.75 hours post-dosing (T_{max}). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{1/2}$) of 8.84 hours. Following a single intravenous dose at 1 mg/kg the initial plasma concentration was 363 ng/ml. The volume of distribution at steady-state (Vss) was 9.3 l/kg and systemic clearance was 1.5 l/h/kg. The elimination $t_{1/2}$ following intravenous dosing was approximately 5.8 h.

During clinical studies maropitant plasma levels conferred efficacy from 1 hour after administration.

The bioavailability of maropitant after subcutaneous administration in dogs was 90.7%. Maropitant displays linear kinetics when administered subcutaneously within the 0.5-2 mg/kg dose range.

Following repeated subcutaneous administration of once-daily doses of 1 mg/kg bodyweight for five consecutive days, accumulation was 146%. Maropitant undergoes cytochrome P450 (CYP) metabolism in the liver. CYP2D15 and CYP3A12 were identified as the canine isoforms involved in the hepatic biotransformation of maropitant.

Renal clearance is a minor route of elimination, with less than 1% of a 1 mg/kg subcutaneous dose appearing in the urine as either maropitant or its major metabolite. Plasma protein binding of maropitant in dogs is more than 99%.

Cats
The pharmacokinetic profile of maropitant when administered as a single subcutaneous dose of 1 mg/kg body weight to cats was characterised by a maximum concentration (C_{max}) in plasma of approximately 165 ng/ml; this was achieved on average 0.32 hours (19 min) post-dosing (T_{max}). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{1/2}$) of 16.8 hours. Following a single intravenous dose at 1 mg/kg the initial plasma concentration was 1040 ng/ml. The volume of distribution at steady-state (Vss) was 2.3 l/kg and systemic clearance was 0.51 l/h/kg. The elimination $t_{1/2}$ following intravenous dosing was approximately 4.9 h. There appears to be an age-related effect on the pharmacokinetics of maropitant in cats with kittens having higher clearance than adults.

During clinical studies maropitant plasma levels conferred efficacy from 1 hour after administration.

The bioavailability of maropitant after subcutaneous administration in cats was 91.3%. Maropitant displays linear kinetics when administered subcutaneously within the 0.25-3 mg/kg dose range.

Following repeated subcutaneous administration of once-daily doses of 1 mg/kg bodyweight for five consecutive days, accumulation was 250%. Maropitant undergoes cytochrome P450 (CYP) metabolism in the liver. CYP1A and CYP3A-related enzymes were identified as the feline isoforms involved in the hepatic biotransformation of maropitant.

Renal and faecal clearances are minor routes of elimination for maropitant, with less than 1% of a 1 mg/kg subcutaneous dose appearing in the urine or faeces as maropitant. For the major metabolite 10.4% of the maropitant dose was recovered in urine and 9.3% in faeces. Plasma protein binding of maropitant in cats was estimated to be 99.1%.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol E1519
Sulfobutylbetadex sodium
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: 3 years.
Shelf life after first opening the immediate packaging: 60 days.

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Amber glass vial type I with bromobutyl rubber stopper and aluminium overseal with flip-off tab.
Cardboard box containing 1 vial of 20 ml.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.

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

KRKA, d.d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

8. MARKETING AUTHORISATION NUMBER

Vm 01656/5038

9. DATE OF FIRST AUTHORISATION

26 October 2023

10. DATE OF REVISION OF THE TEXT

November 2024

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Approved 20 December 2024
Gavin Hall