

*[Version 9.1,11/2024]*

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

### Active substances:

Maropitant 10 mg  
(as maropitant citrate monohydrate)

### Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Metacresol	3.3 mg
Sulfobutylbetadex sodium	
Water for injections	

Clear, colourless to yellow solution.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Dogs, cats

### 3.2 Indications for use for each target species

#### Dogs:

Treatment and prevention of nausea induced by chemotherapy.

Prevention of vomiting except that induced by motion sickness.

Treatment of vomiting, in combination with other supportive measures.

Prevention of perioperative nausea and vomiting and improvement in recovery from general anaesthesia after use of the  $\mu$ -opiate receptor agonist morphine.

#### Cats:

Prevention of vomiting and the reduction of nausea, except that induced by motion sickness.

Treatment of vomiting, in combination with other supportive measures.

### 3.3 Contraindications

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

### 3.4 Special warnings

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).

### **3.5 Special precautions for use**

#### Special precautions for safe use in the target species:

The safety of maropitant 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.

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

The veterinary medicinal product may cause skin sensitization. People with known hypersensitivity to maropitant should administer the veterinary medicinal product with caution. If symptoms occur, such as a rash after accidental exposure, seek medical advice and show the package leaflet or the label to the physician.

Maropitant is a neurokinin-1 (NK1) receptor antagonist that acts in the central nervous system. Accidental self-injection may result in nausea, dizziness and drowsiness. Care should be taken to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

The veterinary medicinal product may be irritant to the eyes. Avoid contact with the eyes. In the case of accidental eye exposure, flush the eyes with plenty of water and seek medical attention. Wash hands after use.

#### Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Dogs, cats:

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

<sup>1</sup> In cats - moderate to severe (in approximately one third of cats) when injected subcutaneously.

<sup>2</sup> In dogs - when injected subcutaneously.

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 safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Use only according to the benefit-risk assessment by the responsible veterinarian.

### 3.8 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.

### 3.9 Administration routes and dosage

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 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.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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 safe use in target species” (section 3.5).

The cap may be safely punctured up to 125 times.

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

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 bodyweight (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.

### **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**

### **3.12 Withdrawal periods**

Not applicable.

## **4. PHARMACOLOGICAL INFORMATION**

### **4.1 ATCvet code : QA04AD90**

### **4.2 Pharmacodynamics**

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 nerve) 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 (NK1) 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 NK1 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.

### **4.3 Pharmacokinetics**

#### 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 ( $V_{ss}$ ) 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 ( $V_{ss}$ ) 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%.

## **5. PHARMACEUTICAL PARTICULARS**

### **5.1 Major incompatibilities**

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

### **5.2 Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 28 months  
Shelf life after first opening the immediate packaging: 84 days

### **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**

20 ml amber polypropylene vial or 50 ml amber multilayer (COEX) PP/HV/EVOH/HV/PP vial closed with bromobutyl rubber stopper and aluminium and plastic flip cap.

Package size:

Cardboard box with 20 ml vial.

Cardboard box with 50 ml vial.

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**

Vet-Agro Multi-Trade Company Sp. z o.o.

### **7. MARKETING AUTHORISATION NUMBER(S)**

### **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 \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).

