10 April 2015
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Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use (CVMP)

CVMP assessment report for Cerenia new route of administration (intravenous use) for the solution for injection (EMEA/V/C/000106/X/0023)

International non-proprietary name: maropitant

Assessment report as adopted by the CVMP with all information of a commercially confidential nature deleted.

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Product profile

Invented name:	Cerenia
Active substance:	Maropitant citrate
Target species:	Cats and dogs
Pharmaceutical form:	Solution for injection
Strength:	10 mg/ml
Therapeutic indication:	**Solution for injection for 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. **Solution for injection for 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.
ATCvet code:	QA04AD90
Pharmacotherapeutic group:	Alimentary tract and metabolism; other antiemetics
Applicant:	Zoetis Belgium SA

Introduction

On 29 August 2014, Zoetis Belgium S.A. submitted an application for an extension to the marketing authorisation for Cerenia to the European Medicines Agency (the Agency) in accordance with Article 19 of Commission Regulation (EC) No. 1234/2008 and Annex I point 2(e) thereof.

The CVMP confirmed C. Friis as rapporteur and E. Persson as co-rapporteur for this application.

Cerenia is an antiemetic product containing maropitant citrate as active substance and was first authorised for use in the European Union (EU) on 29 September 2006. It is available as tablets for dogs and as solution for subcutaneous injection for dogs and cats.

This extension application is for a new route of administration (intravenous use) for the 10 mg/ml solution for injection. The dose (1 mg/kg bodyweight/day up to 5 days) and indications for both target species dogs and cats approved for the solution for injection to be administered subcutaneously remain unchanged.

Cerenia 10 mg/ml solution for injection is authorised for the following indications in dogs and cats:

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 and 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 and for the treatment of vomiting in combination with other supportive measures.

On 10 April 2015, the CVMP adopted an opinion and CVMP assessment report.

On 10 June 2015, the European Commission adopted a Commission Decision for granting an extension to the marketing authorisation for Cerenia.

Part 1 - Administrative particulars

Detailed description of the pharmacovigilance system

The applicant has provided a detailed description of the pharmacovigilance system (version 1.2, dated 18 July 2013) which fulfils the requirements of Directive 2001/82/EC. Based on the information provided the applicant has the services of a qualified person responsible for pharmacovigilance and the necessary means for the notification of any adverse reaction occurring either in the EU or in a third country.

Manufacturing authorisations and inspection status

The active substance, maropitant citrate is manufactured outside the EU. The finished product, Cerenia solution for injection, is manufactured in the EU and outside the EU. Secondary packaging is carried out in the EU. Batch release for the European Union (EU) is carried out by Pfizer PGM, Pocé-sur-Cisse, France.

All relevant sites have valid manufacturing authorisations or valid good manufacturing practice (GMP) certificates, as appropriate.

A satisfactory declaration concerning GMP compliance of the active substance manufacture has been issued by the qualified person at the site of batch release of the finished product. The declaration is issued on the basis of an audit of the site.

Overall conclusions on administrative particulars

The detailed description of the pharmacovigilance system and the GMP certification of the manufacturing sites were considered in line with legal requirements.

Part 2 - Quality

This application does not affect the quality part of the dossier as no changes to the already authorised pharmaceutical form (solution for injection) are made. No new data have been submitted and cross-reference has been made to data that have already been submitted and assessed for previous applications. The CVMP considered this approach acceptable as the pharmaceutical requirements for both routes of administration (subcutaneous and intravenous) for the solution for injection would be identical.

Part 3 – Safety

Safety documentation

An updated environmental risk assessment and target animal tolerance studies have been submitted with this application. Cross-reference has been made to other data that have already been submitted and assessed for previous applications. This is considered acceptable by the CVMP.

Tolerance in the target species of animal

See Part 4.

Environmental risk assessment

An environmental risk assessment (ERA) was provided in accordance with the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) GL6 on environmental impact assessment (EIAs) for veterinary medicinal products (VMPs) - Phase I (CVMP/VICH/592/98-FINAL). Given that the product is for the treatment of companion animals (cats and dogs), the environmental risk assessment can stop at Phase I.

Cerenia solution for injection for dogs and cats is not expected to pose a risk for the environment when used according to the summary of product characteristics (SPC).

User safety

No user safety assessment was supplied to support this application as there are no changes to the already authorised pharmaceutical form or strength. As the risk for the user does not change compared to the already authorised product the CVMP concluded that user safety for this product is acceptable when used as recommended and taking into account the safety advice in the SPC.

Part 4 – Efficacy

Pharmacodynamics

NK_1 receptor antagonists act as broad spectrum antiemetics by inhibiting the binding of substance P in the brain. Maropitant is a potent and selective antagonist of canine and human NK_1 receptors. Studies using ^{3}H-substance P binding in canine striatum indicate that maropitant is an antagonist at the canine receptor with an inhibitory constant (Ki) of 0.5 nM. In contrast, the IC_{50} of maropitant at NK_2 or NK_3 tachykinin receptor subtypes are greater than 1000 nM. Selectivity of maropitant towards inhibiting the binding of substance P is further demonstrated by a lack of activity when tested at high concentrations against a broad range of other neurotransmitters. Maropitant did displace des-methoxy verapamil binding from calcium channels with an IC_{50} = 110 nM. However, free plasma drug concentrations are unlikely to reach those levels in vivo.

The pharmacokinetic data presented together with the affinity data for maropitant at the NK_1 receptor can be used to estimate the duration of antiemetic efficacy. Clinical and laboratory studies indicate that a single dose of maropitant of 1 mg/kg bodyweight (bw) administered subcutaneously provides antiemetic efficacy for 24 hours in the dog. Pharmacokinetic studies indicate that a single dose of 1 mg/kg bw administered subcutaneously results in plasma levels of maropitant of 11.4 nM at 24 h after administration. Because maropitant exhibits 99% plasma protein binding, this corresponds to a free plasma concentration of maropitant of 0.11 nM. Thus, a free plasma concentration of approximately 0.11 nM is necessary to maintain antiemetic activity. Even though 0.11 nM is lower than the Ki of 0.5 nM, it is important to note that active substance levels in the brain stem are likely the determinant for the duration of action of maropitant and data submitted an assessed within other applications of Cerenia indicate a 3 times higher concentration of maropitant in the brain than in plasma.

Pharmacokinetics

Two cross-over bioavailability studies were conducted, one in dogs (A461N-US-13-289) and one in cats (A481N-US-13-080). Both studies were undertaken in the USA in 2014 and were conducted in compliance with good laboratory practice (GLP) standards and the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2). This is considered acceptable by the CVMP.

Dogs

The absolute bioavailability of maropitant citrate was studied in dogs after receiving Cerenia 10 mg/ml solution for injection at a dose of 1 mg/kg bw, given either intravenously or subcutaneously.

Four male and four female clinical healthy Beagle dogs from 9 months to 3 years of age and weighing between 9.3 kg and 11.5 kg were used in a cross-over design. The concentration of maropitant citrate and one of its metabolites in plasma samples was estimated following a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) method. Following intravenous administration maropitant had a fast distribution phase followed by a log-linear elimination. The mean apparent steady state volume of distribution (V_{ss}) was estimated at 9.3 l/kg with a systemic clearance (CL) of 1.51 l/kg/h and a mean residence time (MRT) of 6.2 hours. One of the metabolites of maropitant was detected in 3 of the eight animals at the 3-minute time point. Plasma concentrations of this metabolite were considerably less than those of maropitant. Following subcutaneous administration maropitant quickly (in 0.56 hours) reached a mean peak concentration of 95.3 ng/ml and had complete absorption with a

bioavailability estimate of 108%. The $t_{1/2}$ was 6.0 hours for females and 7.9 hours for males following subcutaneous administration. The significant gender by treatment interaction for $t_{1/2}$ was not evident for any other pharmacokinetic (PK) parameter and is believed to be a spurious finding. The C_{max} of maropitant after intravenous administration was about 3.5 times higher than the concentration after subcutaneous administration whereas the difference between subcutaneous and intravenous administration in the area under the curve (AUC) for maropitant were within the bioequivalence limits ($AUC_{0\text{-}t(last)}$, point estimate 1.08, 90% CI 1.00–1.16). According to the tolerance study in dogs (see below) no adverse reactions were recorded despite the higher initial plasma concentrations noted after intravenous administration. The presence of parent compound in plasma after intravenous and subcutaneous administration is thus similar and covers 24 hours.

Cats

The absolute bioavailability of maropitant citrate was studied in cats after receiving Cerenia 10 mg/ml solution for injection at a dose of 1 mg/kg bw, given either intravenously or subcutaneously. Four male and 4 female clinical healthy short hair cats 6–7 months of age and weighing 2.6–4.4 kg were used in a cross-over design. The concentration of maropitant citrate and of the same metabolite as in the study for dogs in plasma samples was estimated following a validated LC-MS/MS method. Following intravenous administration, maropitant had a fast distribution phase followed by a log-linear elimination. The mean apparent V_{ss} was estimated at 2.3 l/kg with an apparent CL of 0.510 l/kg/h and an MRT of 4.54 hours. The metabolite was detected in 6 of 6 animals treated intravenously at the 3-minute time point. The elimination half-life following intravenous administration was 4.9 hours for maropitant and 17.4 hours for the metabolite. Following subcutaneous administration, maropitant quickly (0.41 hours) reached a mean peak concentration of 229 ng/ml and had nearly complete absorption with a bioavailability estimate of 93%. Similar to intravenous administration, a log-linear elimination phase is apparent following subcutaneous administration. The $t_{1/2}$ was 7.58 hours following subcutaneous dosing for maropitant and 17.6 hours for the metabolite. The C_{max} after intravenous administration was about 4.5 times higher than the concentration after subcutaneous administration. The difference between subcutaneous and intravenous administration in the AUC for maropitant were on borderline within the bioequivalence limits ($AUC_{0\text{-}t(last)}$, point estimate 0.92, 90% CI 0.79–1.08). According to the tolerance study in cats (see below) no adverse reactions were recorded despite the higher initial concentrations after intravenous dosing. The presence of parent compound in plasma after intravenous and subcutaneous administration is thus similar and covers 24 hours.

In conclusion, for both dogs and cats a single bolus of maropitant citrate administered intravenously in a dose of 1 mg/kg bw results in higher C_{max} than when administered subcutaneously, but with comparable AUC. The differences noted are not expected to influence receptor activity. The routes of administration can therefore be considered bioequivalent.

Dose determination/justification

Based on the bioavailability studies, the applicant considered that the same dose as already authorised for the subcutaneous route (1 mg/kg bw once daily up to 5 days) would be efficacious for the intravenous route. This is considered acceptable by the CVMP.

Target animal tolerance

Target animal safety was demonstrated by the applicant by two new laboratory target animal safety studies, one in dogs and one in cats as well as by a review of pharmacovigilance data for the already

authorised solution for injection. In addition, a literature review was provided on the tolerance of intravenous administration of the excipients (meta-cresol and sulfobutylether beta-cyclodextrin; SBECD), and an in vitro haemolysis study.

The two pivotal target animal safety studies were undertaken in the USA during 2013 and 2014.

Dogs (#A366N-US-13-276)

Cerenia solution for injection was administered once daily as bolus (slow push over 1–2 minutes) via intravenous injection for 5 consecutive days to 2 groups (groups T02 and T03) of Beagle dogs of 16 weeks of age. Dose levels were 1 mg/kg bw and 3 mg/kg bw (1X and 3X the recommended therapeutic dose, RTD) for groups T02 and T03, respectively. A concurrent control group (group T01) received 0.9% (w/v) sodium chloride for injection on a comparable regimen. Each group consisted of 4 males and 4 females. Following 5 days of dose administration, all animals were euthanised. Results showed no test article-related effects on survival or clinical findings. In addition, there were no test article-related macroscopic or microscopic findings, effects on body weight, food consumption or alterations in haematology, coagulation, or serum chemistry parameters. Localised gross necropsy observations and microscopic changes at the injection site were observed in the control and test article-treated groups and were considered to be a result of the dose administration procedures (intravenous injection) and not a direct result of the test article. It is concluded that Cerenia solution for injection administered intravenously at 1X and 3X the nominal dose to dogs once daily for 5 days was well tolerated with no clinically significant findings.

The potential for cardiac related adverse reactions was thoroughly evaluated for the dog in conjunction with the original authorisation of Cerenia, in light of an observed decrease in heart rate and increased QTc intervals in dogs and humans related to maropitant exposure. A specific cardiac safety study was previously assessed where dogs were provided a single oral dose of up to 24 mg/kg bw. The results indicated some changes to the electrocardiogram patterns which however, were not considered to be toxicologically or clinically relevant. Receptor affinity studies presented in the initial marketing authorisation application suggested that with regard to potential blocking of ion channels in the heart this may occur during presence of maropitant at higher plasma levels (µM). However, according to the PK data generated for the current application, the highest plasma concentrations that will be reached during intravenous administration are about 7.5 nM for the dog and 20 nM for the cat, which would suggest a small risk for ion receptor interaction of clinical significance for cardiac function for both species. In the cardiac safety study submitted within the initial marketing authorisation application where dogs were given up to 24 mg maropitant/kg bw orally, plasma levels were not assessed. However, in other studies provided by the applicant for previous applications of Cerenia, oral administration of 20 mg/kg bw to dogs (assuming 99% plasma protein binding) resulted in a free peak plasma concentration of 39 nM, without showing any impact on cardiac functions. Consequently, it can be assumed that the risk for cardiac affection is also low during intravenous treatment at the recommended dose. The tolerance studies presented in the current application did not involve any evaluation of cardiac function and the monitoring schedule did not involve frequent clinical assessment during the first period after treatment, which is a deficiency. However, no clinically relevant adverse events were noted. In addition, the SPC includes already a warning that Cerenia should be used with caution in animals suffering from or with predisposition for cardiac diseases. Given the previous information available regarding cardiac safety, the studies are regarded sufficient to conclude on acceptable tolerance for the intravenous administration route.

Following subcutaneous injection, the most common adverse event is moderate to severe pain at the injection site. No such reactions were noted following administration via the intravenous route.

Cats (#A386N-US-13-077)

Cerenia solution for injection was administered once daily via intravenous (slow push over 1–2 minutes) injection for 5 consecutive days to 2 groups (groups T02 and T03) of domestic shorthair cats. Dose levels were 1 mg/kg bw and 3 mg/kg bw (1X and 3X the recommended therapeutic dose) for groups T02 and T03, respectively. A concurrent control group (group T01) received 0.9% (w/v) sodium chloride for injection on a comparable regimen. Each group consisted of 4 males and 4 females. Following 5 days of dose administration, all animals were euthanised.

Results showed no test article-related effects on survival or clinical findings. In addition, there were no test-article related macroscopic or microscopic findings, effects on bodyweight, food consumption, or alterations in haematology, coagulation, or serum chemistry parameters. Localised gross necropsy observations and microscopic changes at the injection site were observed in the control and test article-treated groups and were considered to be a result of the dose administration procedures (intravenous injection) and not a direct result of the test article.

Similarly to the tolerance study in dogs, the monitoring schedule did not involve frequent clinical assessment during the first period after treatment, which is a deficiency. However, no adverse events related to the new route of administration were indicated and it could be acceptable to conclude on sufficient cardiac safety for intravenous administration on the basis of the information available for the dog species. In addition, the SPC includes already a warning that Cerenia should be used with caution in animals suffering from or with predisposition for cardiac diseases.

It is concluded that Cerenia solution for injection administered intravenously at 1X and 3X the nominal dose to cats once daily for 5 days was well tolerated with no clinically significant findings. Following subcutaneous injection, a very common adverse event in cats is moderate to severe pain at the injection site. No such reactions were noted following administration of Cerenia via the intravenous route.

Field trials

No new studies have been provided. As bioequivalence was demonstrated between intravenous and subcutaneous administration, this was considered acceptable by the CVMP.

Other studies

Tolerance of excipients

The safety assessment of intravenous administration of meta-cresol and sulfobutylether beta-cyclodextrin (SBECD) as excipients in the Cerenia formulation is based on a literature review of available toxicology information and on actual daily doses of those excipients to the target animal (dog and cat). The actual doses (mg/kg) of excipients resulting from intravenous administration of Cerenia to dogs and cats at the RTD of 1 mg/kg bw daily for 5 days are well below doses shown to be toxic in published literature for other species. It is therefore concluded that no further studies on the safety or tolerance of SBECD or m-cresol in either dogs or cats are required when Cerenia is administered intravenously at the proposed dose.

In vitro haemolysis study (Study 13ZOETP1R2)

In one of the previous studies presented by the applicant for the authorisation of Cerenia for dogs, 4 out of 8 dogs dosed intravenously with 8 mg maropitant/kg bw (dissolved in 10% ethanol in 0.9% (w/v) vehicle) had shown evidence of haemolysis. This reaction had not been seen in the dogs dosed with the

same quantities of ethanol but a lower dose of maropitant (1 and 2 mg/kg bw) suggesting the effect seen was a result of the higher concentration of maropitant administered rather than an effect of the ethanol vehicle. Evidence in the literature suggests that ethanol can potentiate the haemolytic potential of some drugs. This in vitro study was performed to test whether this explanation is plausible.

Heparinised pooled samples of blood from 3 male adult Beagles (0.9 ml) was added to plastic tubes and incubated with 0.1 ml of various test formulations: (i) 0.9% (w/v) saline (negative control); (ii) 2% sodium dodecyl sulfate (positive control); (iii) 8 mg/ml maropitant in 10% ethanol in 0.9% (w/v) saline; (iv) 2 mg/ml maropitant in 10% ethanol in 0.9% (w/v) saline; (v) 10 mg/ml maropitant in 6.3% SBS-b-CD, 0.33% m-cresol in water for injection (excipients in Cerenia); (vi) 10% ethanol in 0.9% (w/v) saline; (vii) 6.3% SBS-b-CD, 0.33% m-cresol in water for injection. After incubation and wash the intact red cells were harvested and lysed by sterile water. The amount of haemoglobin released into the water was quantified by measuring the absorbance at 540 nm in a spectrophotometer. The results showed that maropitant in 10% ethanol in 0.9% (w/v) saline gave a concentration dependent haemolysis (92.6% at 8 mg/ml and 20.2% at 2 mg/ml) whereas ethanol alone gave 9.3% haemolysis and maropitant (10 mg/ml) in the vehicle contained in Cerenia gave 7.6% haemolysis. The Cerenia vehicle alone gave 0% haemolysis. It is therefore concluded that the formulations of maropitant in ethanol showed borderline or actual haemolysis, whereas the Cerenia formulation of maropitant was non-haemolytic.

Pharmacovigilance data

The applicant has presented data from their Global PV Works Pharmacovigilance Database relating to extra-label use of Cerenia in dogs and cats by the intravenous route. As of March 2013 the database contained 223 reports of intravenous use of Cerenia in dogs and cats, the majority of which were from the USA (217) and involved 216 dogs and 7 cats. Combining the data from the USA and the rest of the world, 26 cases had one or more clinical signs. The most common clinical sign was pain on injection (5 of 26) which probably suggests extravascular injection. None of the 26 cases showing clinical signs were classified as A ("probably related to treatment").

Overall conclusion on efficacy

The new pharmacokinetic/bioequivalence studies using Cerenia solution for injection in both dogs and cats have clearly characterised the plasma concentration versus time profiles for maropitant citrate and its major metabolite following intravenous administration in comparison with those obtained following subcutaneous administration. For both species the systemic exposure achieved with intravenous dosing is very similar to that achieved with subcutaneous administration except immediately after administration where the drug is distributed from blood to the body organs. No adverse reactions were observed at that period. In account of comparable plasma concentration time profiles the dose is considered to be sufficiently supported. The absence of dose finding studies is therefore justified.

In two new laboratory target animals safety studies, Cerenia solution for injection, administered intravenously at 1X or 3X the recommended dose once daily for 5 days, was well tolerated with no clinically significant findings in either Beagle dogs or domestic short hair cats. The actual doses (mg/kg) of excipients resulting from intravenous administration of Cerenia to dogs and cats at the current label dosage of 1 mg/kg bw daily for 5 days are well below the doses shown to be toxic in published literature for other species. In an in vitro assay of haemolytic potential, maropitant as formulated in Cerenia solution for injection was not haemolytic.

The four new laboratory studies presented with this application together with the literature review on toxicity of excipients and the in vitro haemolysis study provide complementary data to that already submitted by the applicant in support of this product. The new data presented, together with that

previously presented provide sufficient evidence that Cerenia solution for injection at a dose of 1 mg/kg bw daily for 5 days could be used safely intravenously in dogs and cats to produce the equivalent efficacy to the product when administered by the subcutaneous (dogs and cats) and oral (dogs) routes.

Since the intravenous administration of Cerenia is intended to be used in dehydrated patients who require fluid therapy and where the absorption of the drug from subcutis is expected to be reduced one could speculate that the veterinarian would dissolve the dose in the fluid for infusion. However, in the absence of any compatibility studies with such fluids, a warning has been included in the SPC to indicate that Cerenia should be given as a single bolus once daily up to 5 days without mixing the product with any other fluids.

Part 5 – Benefit-risk assessment

Introduction

Cerenia is an antiemetic product containing maropitant citrate as active substance and was first authorised for use in the EU on 29 September 2006. It is available as tablets for dogs and as solution for subcutaneous injection for dogs and cats for the treatment and/or prevention of vomiting caused by different reasons.

This extension application is for a new route of administration (intravenous use) for the solution for injection. The indications and recommended dose remain unchanged compared to those already authorised for subcutaneous use.

Benefit assessment

Direct therapeutic benefit

The benefit of Cerenia 10 mg/ml solution for injection for intravenous use relates to its efficacy.

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.

The recommended treatment dose is a once daily intravenous injection of 1 mg/kg bw (1 ml/10 kg bw) for up to 5 consecutive days in both dogs and cats.

The efficacy of the product in the proposed dose and dosing interval has been confirmed in two bioequivalence studies, one in dogs and one in cats, where Cerenia 10 mg/ml solution injected subcutaneously was used as the reference treatment.

Additional benefits

Cerenia 10 mg/ml solution for injection administrated intravenously is of value in the treatment of dehydrated patients as it would be standard practice to place an intravenous fluid line to these animals. Additionally, the most common adverse event shown with subcutaneous administration (pain at injection site) is avoided by the administration of the product intravenously.

Risk assessment

Main potential risks have been identified as follows:

For the target animal:

Since the intravenous administration of Cerenia is intended to be used in dehydrated patients that require fluid therapy and where the absorption of the drug from subcutis is expected to be reduced there is the risk that the veterinarian would dissolve the dose in the fluid for infusion. In the absence of any compatibility studies with such fluids, a warning has been included in the SPC to indicate that Cerenia should be given as a single bolus once daily up to 5 days without mixing the product with any other fluids.

For the user:

The risk for the user does not change compared to the already authorised product as there are no changes to the pharmaceutical form or strength. The CVMP concluded that user safety for this product is acceptable when used as recommended and taking into account the safety advice in the SPC.

For the environment:

The product is not expected to pose a risk for the environment when used according to the SPC.

Risk management or mitigation measures

Appropriate information has been included in the SPC to inform on the potential risks of this product relevant to the target animal, user and the environment, and to provide advice on how to prevent or reduce these risks.

Evaluation of the benefit-risk balance

Cerenia 10 mg/ml solution for injection administered intravenously has shown to have a positive benefit-risk balance overall

It is well tolerated by the target animals and presents an acceptable risk for users and the environment when used as recommended and appropriate warnings have been included in the SPC.

Conclusion on the benefit-risk balance

The overall benefit-risk evaluation for the product is deemed positive with a sufficiently clear and complete product information.

Conclusion

Based on the original and complementary data presented the CVMP concluded that the quality, safety and efficacy of Cerenia 10 mg/ml solution for injection for dogs and cats administered intravenously are considered to be in accordance with the requirements of Directive 2001/82/EC.

Based on the CVMP review of the data on quality, safety and efficacy, the CVMP recommends the extension of the marketing authorisation for Cerenia to add a new route of administration (intravenous use) for Cerenia 10 mg/ml solution for injection for dogs and cats.