IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Prinocate 250 mg/62.5 mg spot-on solution for large dogs

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PRODUCT SUMMARY

EU Procedure number	IE/V/0392/005/DC
Name, strength and pharmaceutical form	Prinocate 250 mg/62.5 mg spot-on solution for large dogs
Active substances(s)	Imidacloprid,Moxidectin
Applicant	Krka, d.d., Novo mesto Šmarješka cesta 6 8501 Novo mesto Slovenia
Legal basis of application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Date of completion of procedure	20/11/2019
Target species	Dogs
Indication for use	For dogssuffering from, or at risk from, mixed parasitic infections: The treatment and prevention of flea infestation (*Ctenocephalides felis*), The treatment of biting lice (*Trichodectes canis*), The treatment of ear mite infestation (*Otodectes cynotis*), sarcoptic mange (caused by *Sarcoptes scabiei* var. *canis*), demodicosis (caused by *Demodex canis*), The prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*), Treatment of circulating microfilariae (*Dirofilaria immitis*), The treatment of cutaneous dirofilariosis (adult stages of *Dirofilaria repens*), The prevention of cutaneous dirofilariosis (L3 larvae of *Dirofilaria repens*), The reduction of circulating microfilariae (*Dirofilaria repens*), The prevention of angiostrongylosis (L4 larvae and immature adults of *Angiostrongylus vasorum*), The treatment of *Angiostrongylus vasorum* and *Crenosoma vulpis*, The prevention of spirocercosis (*Spirocerca lupi*), The treatment of *Eucoleus* (syn. *Capillaria*) *boehmi* (adults), The treatment of the eye worm *Thelazia callipaeda* (adults), Treatment of infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocara canis, Ancylostoma caninum* and *Uncinaria stenocephala*, adults of *Toxascaris leonina* and *Trichuris vulpis*). The product can be used as part of a treatment strategy for flea allergy dermatitis (FAD).
ATCvet code	QP54AB52
Concerned Member States	AT, BE, BG, CY, CZ, EE, EL, ES, FR, HR, HU, IT, LT, LV, NL, PL, PT, RO, SK, SI, UK

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PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
It has been shown that the product can be safely used in the target species; the slight reactions observed are indicated in the SPC.
The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains the active substances imidacloprid and moxidectin and the excipients benzyl alcohol (E 1519), propylene carbonate, butylhydroxytoluene (E 321) and trolamine. The container/closure system consists of a white polypropylene (PP) unit dose pipette with a closure with a spike composed of high density polyethylene (HDPE) or polyoxymethylene (POM) or polypropylene (PP) packed into a laminated triplex bag composed of polyester (PETP), aluminium (Al) and low density polyetylene (LDPE).

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

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C. Control of Starting Materials

The active substances imidacloprid and moxidectin are established active substances described in the European
Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with their specifications have been provided.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

D. Control on Intermediate Products

Not applicable.

E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods has been provided.
Batch analytical data from the proposed production site<s> has been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substances has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances when stored under the approved conditions.

Stability data on the finished product has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

The application has been submitted in accordance with paragraph 3 of Article 13 of Directive 2001/82/EC, as amended (a hybrid veterinary medicinal product). The reference veterinary medicinal product is Advocate 250 mg + 62.5 mg spot on solution for large dogs containing imidacloprid and moxidectin.

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III. SAFETY ASSESSMENT

Pharmacological Studies

It was claimed that the product has the same qualitative and quantitative composition of active ingredient and excipients as the reference veterinary medicinal product, Advocate 250 mg + 62.5 mg spot on solution for large dogs (i.e. it is claimed to be identical).
Both products are spot-on solutions and they are used in the same species, for the same indications, in the same doses and using the same administration method. The applicant claimed that the candidate formulation is identical to that of the reference product, Advocate 250 mg + 62.5 mg spot on solution for large dogs, based upon the results of comparative studies conducted using the reference product and the candidate formulation, including a comparison of physicochemical properties. The applicant has demonstrated that the candidate product is qualitatively and quantitatively sufficiently similar to be considered the same as the reference product in terms of the active substances (imidacloprid and moxidectin), and the excipients.
Hence bioequivalence can be assumed and in vivo bioequivalence studies are not required. Given that bioequivalence with the authorised reference product can be accepted and that the test product is intended to be administered to the same target species, using the same routes of administration at the same dose rates as already approved for the reference product, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials.

Toxicological Studies

This is a hybrid application in accordance with parargraph 3 of Article 13 and as bioequivalence with a reference product is accepted, results of toxicological tests are not required. The safety aspects of this product are expected to be the same as those of the reference product. Warnings and precautions as listed on the product literature are broadly in line with those of the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the risk to the user associated with this product is the same as that of the reference product. The proposed user safety statements are broadly in line with those of the reference product and are generally acceptable. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:
In order to prevent children from getting access to pipettes, keep the pipette in the original packaging until ready for use and dispose of used pipettes immediately.
Do not ingest. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
People with a known hypersensitivity to benzyl alcohol, imidacloprid or moxidectin should administer the product with caution. In very rare cases the product may cause skin sensitisation or transient skin reactions (for example numbness, irritation or burning/tingling sensation).
In very rare cases the product may cause respiratory irritation in sensitive individuals.
If the product accidentally gets into eyes, they should be thoroughly flushed with water.
Avoid contact with skin, eyes or mouth.
In case of accidental spillage onto skin, wash off immediately with soap and water.
Wash hands thoroughly after use.
If skin or eye symptoms persist, seek medical advice immediately and show the package leaflet or label to the physician.
Do not eat, drink or smoke during application.
Treated animals should not be handled, especially by children, until the application site is dry. Therefore, it is recommended to apply the product in the evening. Recently treated animals should not be allowed to sleep in the same bed as their owner, especially children.

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The solvent in the product may stain or damage certain materials including leather, fabrics, plastics and finished surfaces. Allow the application site to dry before permitting contact with such materials.
The product should not enter water courses as it has harmful effects on aquatic organisms: moxidectin is highly toxic to aquatic organisms. Dogs should not be allowed to swim in surface waters for 4 days after treatment.

Environmental Risk Assessment

Environmental Risk Assessment Phase I The environmental risk assessment can stop in Phase I, Question No. 3, because the medicine will be used only in non-food animals. It is accepted that the environmental safety statements agreed for the reference product can be applied to this product. **Conclusion**
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

As this is a hybrid application in accordance with paragraph 3 of Article 13 and bioequivalence with a reference product is accepted, efficacy studies are not required. The efficacy claims for this product are expected to be equivalent to those of the reference product. In addition, it is considered that the risk to the target species will be similar for both the test and the reference products. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

V. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the HPRA website.
This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

Changes:

None

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