IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Moxiclear 100 mg + 25 mg spot-on solution for medium dogs

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PRODUCT SUMMARY

Name, strength and pharmaceutical form	Moxiclear 100 mg + 25 mg spot-on solution for medium dogs
Active substance(s)	Imidacloprid Moxidectin
Applicant	Norbrook Laboratories (Ireland) Limited, Rossmore Industrial Estate, Monaghan, Ireland
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation	29th March 2018
Target species	Medium dogs
Indication for use	**For dogs suffering from,or at risk from, mixed parasitic infections:** • For 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*), , • the prevention of heartworm disease (L3 and L4 larvae of *Dirofilaria immitis*), • the 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

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	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 infections with gastrointestinal nematodes (L4 larvae, immature adults and adults of *Toxocaracanis, 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

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.

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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. Composition

Each pipette contains 100 mg imidacloprid and 25 mg moxidectin and the excipients butylhdroxytoluene, propylene carbonate and benzyl alcohol.
The product is presented as a:
1.0 ml clear pipette with a film composed of 3 layers: a polypropylene/COC, solvent free lacquer laminate and a copolymer of polyethylene/EVOH/polyethylene. The pipettes are sealed within a child resistant 4-ply foil sachet composed of LDPE/nylon/aluminium foil/polyester film and presented in an outer box (boxes of 1, 2, 3, 4, 6, 9, 12, 21 or 42 pipettes). Each pipette is individually sealed in a foil sachet.

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 on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances are imidacloprid and moxidectin both of which are established active substances. 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 these specifications have been provided.

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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 have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substances have 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 have 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

None.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This was a generic application submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The reference veterinary medicinal product is Advocate Spot-On for dogs – containing imidocloprid and moxidectin.

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III.A Safety Testing 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 Spot-On (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 claim that Moxiclear can be considered identical to the reference product was based on a comparison of the qualitative and quantitative composition of both products, including a comparison of physicochemical properties. Based on this data, an exemption from the requirement to conduct an *in vivo* bioequivalence study was justified in accordance with current guidance, section 7.1(b)

of EMA/CVMP/016/00-Rev2 (Guideline on the conduct of bioequivalence studies for veterinary medicinal products):

For products intended for intramuscular, subcutaneous or systemically acting topical administration, bioequivalence studies are not required in cases when the product is of the same type of solution, contains the same concentration of the active substance and comparable excipients in similar amounts as the reference veterinary medicinal product, if it can be adequately justified that difference(s) in the excipient(s) and/or their concentration have no influence on the rate and/or extent of absorption of the active substance.

and section 7 of EMEA/CVMP/EWP/005/2000-Rev.3 (Guideline for the testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestation in dogs and cats).

Based on the data/information provided, the test product can be accepted as a generic of the reference product and, consequently, the applicant is not required to provide the results of safety tests or of pre-clinical and clinical trials.

Toxicological Studies

As this is a generic application according to Article 13 (1), 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 identical to 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 identical to 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:

- Avoid contact with skin, eyes or mouth.

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- Do not eat, drink or smoke during application. Wash hands thoroughly after use.
- After application do not stroke or groom animals until the application site is dry.
- In case of accidental spillage onto skin, wash off immediately with soap and water.
- People with 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.
- If skin or eye symptoms persist, or the product is accidentally swallowed, seek medical advice immediately and show the package leaflet or the label to the physician.
- Do not ingest. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. 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. Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.
- 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.

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 acknowledged that moxidectin may be toxic to aquatic organisms and 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.

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IV. CLINICAL ASSESSMENT

See **Part III.A**
As this is a generic application according to Article 13 (1), 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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