# IPAR

# Publicly Available Assessment Report for a Veterinary Medicinal Product

Eprecis 5 mg/ml pour-on solution for cattle

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## PRODUCT SUMMARY

| | |
|---|---|
| EU Procedure number | IE/V/0343/001/DC |
| Name, strength and pharmaceutical form | Eprecis 5 mg/ml pour-on solution for cattle |
| Active substance(s) | Eprinomectin |
| Applicant | CEVA Santé Animale,<br>10, Avenue de la Ballastière,<br>33500 Libourne,<br>FRANCE. |
| Legal basis of application | Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended. |
| Date of completion of procedure | 22/04/2015 |
| Target species | Cattle (beef and dairy cattle). |
| Indication for use | Treatment of infestations by listed internal and external parasites sensitive to eprinomectin, and the prevention of reinfestation against listed internal parasites. |
| ATCvet code | QP54AA04 |
| Concerned Member States | BE, DK, FR, DE, HU, IT, NL, PL, PT, ES, UK |

## 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 product is safe for the user, the consumer of foodstuffs from treated animals 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.

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# II QUALITY ASPECTS

## *A. Qualitative and Quantitative Particulars*

The product contains eprinomectin (5 mg/ml) and the excipients butylhydroxytluene (E321), all-rac- -Tocopherol (E307) and propylene gycol dicaprylocaprate.
The product is presented in a 250 ml translucent high density polyethylene (HDPE) bottle with 10 ml dispenser and removable aluminium/PE seals and PE screw caps or alternatively a 1L, 2.5 L or 5L white HDPE bottle, with a removable aluminium/PE seal and a polypropylene (PP) screw cap.

The choice of the formulation is justified.

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.

## *C. Control of Starting Materials*

The active substance is eprinomectin an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification has 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 has been provided demonstrating compliance with the specification.

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### *F. Stability*

Stability data on the active substance has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance 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)

### *III.A Safety Testing*

***Pharmacological Studies***

This application was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended (that is, a "generic" application). The reference product is *Eprinex 0.5% w/v Pour-On Solution for Beef and Dairy Cattle* (Merial Animal Health, VPA 10857/003/001), which has been authorised in the Community for greater than 10 years.

On the basis of appropriate comparative analysis, it is accepted that the test and reference products are identical in terms of both active substance and excipients, Accordingly, the omission of bioequivalence studies can be considered justified as per EMEA/CVMP/016/00-Rev2 ("Guideline on the conduct of bioequivalence studies for veterinary medicinal products"), Chapter 7.1 (b):

> "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 and comparable excipients in similar amounts as the reference veterinary medicinal product, if it can be adequately justified that the 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."

As bioequivalence with an authorised reference product is accepted, the applicant is not required to provide the results of the safety and residue tests or of the pre-clinical and clinical trials. Both the test and reference products can be expected to have the same safety and efficacy profile.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

***User Safety***

Given that the test and reference products are identical in terms of both composition and intended use, it is argued that the user safety profile will be the same for both products and that the user safety statements agreed for the reference product can be applied to the test product. The following user safety statements are proposed for inclusion in the SPC:

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Avoid direct contact with the skin or eyes.

Wear rubber gloves and protective clothing when applying the product.

If accidental skin contact occurs, wash the affected area immediately with soap and water.

If accidental eye exposure occurs, flush eyes immediately with water.

Do not smoke or eat while handling the veterinary medicinal product.

Wash hands after use. Should clothing become contaminated, remove as soon as possible and launder before re-use. In the event of ingestion, wash out mouth with water and seek medical advice.

People with known hypersensitivity to the active substance or to any of the excipients should avoid contact with the veterinary medicinal product.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

***Environmental Risk Assessment***

A Phase II ERA is required as the target species are reared on pasture, and eprinomectin is an endo- & ectoparasiticide.

The applicant provided a comprehensive data package on the environmental fate and toxicity of eprinomectin. Using those study data, the applicant presented a detailed ERA. The risk assessment highlights potential risks for:

dung dwelling organisms exposed to dung produced by treated pasture animals;

certain aquatic organisms in surface water in the case of direct excretion and indirect exposure from run-off events; and certain organisms in sediment in the case of

direct excretion.

The risks identified are as expected for this class of compound (macrocyclic lactones) and, with a view to reducing the risk identified, risk mitigation measures similar to those accepted for related product have been included in the SPC and on product labelling.

## *III.B Residues Documentation*

***Residue Studies***

As this is a generic application according to Article 13(1), no residue depletion studies were conducted/presented. Given that the test and reference products are identical in terms of both composition and intended use, the residue depletion profile will be the same for both products and the withdrawal periods agreed for the reference product can be applied to the test product.

***MRLs***

Eprinomectin is listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

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| | Bovine |
|---|---|
| Muscle | 50 µg/kg |
| Liver | 1500 µg/kg |
| Kidney | 300 µg/kg |
| Fat | 250 µg/kg |
| Milk | 20 µg/kg |

***Withdrawal Periods***

Based on the argumentation presented, withdrawal periods of 15 days for meat in cattle and zero hours for milk are justified.

## IV CLINICAL ASSESSMENT (EFFICACY)

### *IV.A Pre-Clinical Studies*

This application was submitted in accordance with Article 13(1) of Directive 2001/82/EC, as amended (that is, a "generic" application). The reference product is Eprinex 0.5% w/v Pour-On Solution for Beef and Dairy Cattle (Merial Animal Health, VPA 10857/003/001).

Based on the information provided, bioequivalence with the authorised reference product is accepted (products are identical in terms of both composition and intended use). Accordingly, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials.

Given that bioequivalence is accepted, both the test and reference products can be expected to have the same profile in terms of both target animal safety and efficacy. The proposed indications and posology reflect those agreed for the authorised reference product.

***Resistance***

Adequate warnings and precautions appear on the product literature:

Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:

- Too frequent and repeated use of anthelmintics from the same class, over an extended period of time.
- Underdosing, which may be due to underestimation of body weight, misadministration of the product, or lack of calibration of the dosing device (if any).

Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. Faecal Egg Count Reduction Test). Where the results of the test(s) strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used.

To date no resistance to eprinomectin (a macrocyclic lactone) has been reported within the EU. However resistance to other macrocyclic lactones has been reported in parasite species in cattle within the EU. Therefore, use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

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### *Tolerance in the Target Species of Animals*

A target animal safety study specific to the test product has not been presented with the application. Given that bioequivalence is accepted on the basis of identical composition, both the test and reference products can be expected to have the same profile in terms of target animal safety.

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

### *IV.B Clinical Studies*

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. No proprietary efficacy studies have been carried out. The applicant has confirmed that the proposed product has the same qualitative and quantitative composition to that of the reference product. Consequently, efficacy studies relating to the test product are not required.

The efficacy claims for this product are equivalent to those of the reference product.

## 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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