MINISTERIO DE SANIDAD
agencia española de medicamentos y productos sanitarios

DEPARTAMENTO DE MEDICAMENTOS VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

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28022 – Madrid
España
(Reference Member State)

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

EPRINOVET MULTI 5 mg/ml pour-on solution for cattle, sheep and goats

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PRODUCT SUMMARY

EU procedure number	ES/V/0443/001/DC
Name, strength and pharmaceutical form	EPRINOVET MULTI 5 mg/ml pour-on solution for cattle, sheep and goats
Applicant	Laboratorios Calier S.A.
Active substance	Eprinomectin
ATC vetcode	QP54AA04
Target species	Cattle (beef and dairy cattle), sheep and goats
Indication for use	Treatment of infestation by the following parasites: **Cattle:**

Parasite	Adult	L4	Inhibited L4
Gastrointestinal Roundworms			
Ostertagia spp.	♦	♦	
Ostertagia lyrata	♦		
Ostertagia ostertagi	♦	♦	♦
Cooperia spp.	♦	♦	♦
Cooperia oncophora	♦	♦	
Cooperia punctata	♦	♦	
Cooperia surnabada	♦	♦	
Cooperia pectinata	♦	♦	
Haemonchus placei	♦	♦	
Trichostrongylus spp.	♦	♦	
Trichostrongylus axei	♦	♦	
Trichostrongylus colubriformis	♦	♦	
Bunostomum phlebotomum	♦	♦	
Nematodirus helvetianus	♦	♦	
Oesophagostomum spp.	♦		
Oesophagostomum radiatum	♦	♦	
Trichuris spp.	♦		
Lungworms			
Dictyocaulus viviparus	♦	♦	

Warbles (parasitic stages)
Hypoderma bovis
Hypoderma lineatum

Mange mites
Chorioptes bovis
Sarcoptes scabiei var. bovis

Lice
Linognathus vituli
Damalinia bovis
Haematopinus eurysternus
Solenopotes capillatus

Flies
Haematobia irritans

PROLONGED ACTIVITY
Applied as recommended, the product prevents reinfestations with

Parasite	Prolonged Activity
Dictyocaulus viviparus	Up to 28 days
Ostertagia ostertagi	Up to 28 days
Oesophagostomum radiatum	Up to 28 days
Cooperia punctata	Up to 28 days
Cooperia surnabada	Up to 28 days
Cooperia oncophora	Up to 28 days
Nematodirus helvetianus	Up to 14 days
Trichostrongylus colubriformis	Up to 21 days
Trichostrongylus axei	Up to 21 days
Haemonchus placei	Up to 21 days

For best results the veterinary medicinal product should be part of a programme to control both internal and external parasites of cattle based on the epidemiology of these parasites.

Sheep:
Gastrointestinal roundworms (adults)
Teladorsagia circumcincta (pinnata/trifurcata)
Haemonchus contortus
Trichostrongylus axei
Trichostrongylus colubriformis
Nematodirus battus
Cooperia curticei
Chabertia ovina
Oesophagostomum venulosum

Lungworm (adult)
Dictyocaulus filaria

Nasal Bots (L1, L2, L3)
Oestrus ovis

Goats:
Gastrointestinal roundworms (adult)
Teladorsagia circumcincta (pinnata/trifurcata)
Haemonchus contortus
Trichostrongylus axei
Trichostrongylus colubriformis
Nematodirus battus
Cooperia curticei Oesophagotomum venulosum

Lungworm (adult)
Dictyocaulus filaria

Nasal Bots (L1, L2, L3)
Oestrus ovis

Warbles (L1, L2, L3)
Przhevalskiana silenus

For best results the veterinary medicinal product should be part of a programme to control both internal and external parasites of sheep and goats based on the epidemiology of these parasites.

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Hybrid application in accordance with Article 19.1 of Regulation (EU) 2019/6 as amended.
Reference product (RP)	Eprinex Multi 5 mg/ml pour on solution for cattle, sheep and goats
Marketing authorisation holder	Boehringer Ingelheim Vetmedica GmbH
MS where the RP is or has been authorised	ES
Marketing authorisation number	3469 ESP
EU procedure number	IE/V/0347/001/DC
Date of authorisation	27/09/2016
Date of completion of the original decentralised procedure	30/04/2025
Date veterinary medicinal product first authorised in the Reference Member State (MRP only)	-
Concerned Member States for original procedure	HR, FR, EL, IT, SK, PT, RO
Concerned Member States for subsequent recognition procedure	-
Withdrawn CMS during original <mutual recognition> <decentralised><subsequent recognition> procedure	-

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP 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 VMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

2.A. Product description

The VMP contains eprinomectin *(5 mg/ml) and the excipients butylhydroxytoluene and propylene glycol dicaprylocaprate*.

The container/closure system is an white high-density polyethylene (HDPE) bottle sealed with a wax/polyolefin seal and closed with a white polypropylene screw cap.

Details of the device with which the VMP will be used/administered are provided, as applicable.

The choice of the excipient and formulation are justified.

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

2.B. Description of the manufacturing method

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

Process validation data on the VMP have been presented in accordance with the relevant European guidelines.

2.C. Production and control of starting materials

The active substance is eprinomectin, an established substance described in the USP. 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 have been provided.

Certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

2.D. Control tests carried out on isolated intermediates during the manufacturing process

Not applicable.

2.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 VMP.

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.

2.F. Stability tests

A re-test period is set in the ASMF of the active substance.

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

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of pharmacological and toxicological tests are not required.

3.A. Safety tests

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that the risks associated with the candidate product are the same as those of the reference product.

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

Environmental Risk Assessment

A Phase I and Phase II environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

A Phase II ERA is required as the VMP is an ectoparasiticide and endoparasiticide for cattle, sheep and goat and the target animals are reared on pasture.

Phase II:

A Phase II data set was provided according to the requirements of the CVMP/VICH guideline GL38 and the CVMP guideline on the Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-Rev.1), The data were considered to be complete and acceptable.

Physical-chemical properties			
Study type	Test protocol	Result	Remarks
Water solubility	OECD 105	21.9 mg/L	
Dissociation constants in water pKa	OECD 112	No dissociation at environmentally relevant pH (pH 0.1 – 13.9)	
n-Octanol/Water Partition Coefficient logP_{ow}	OECD 117	Log Pow Eprinomectin B1a = 5.4 Log Pow Eprinomectin B1B = 4.8	

Environmental fate			
Soil Adsorption/Desorption	OECD 106	Silty loam (Soil 1) Koc = 2750 l/kg Silty loam (soil 2) Koc = 1000 l/kg Loamy sand (Soil 3) Koc = 4790 l/kg	
Aerobic and Anaerobic Transformation in Soil	OECD 307	Refesol-02A: DT50 soil, [SFO], [20ºC] = 142 d LUFA 2.2: DT50 soil, [SFO], [20ºC] = 125 d LUFA 2.3: DT50 soil, [SFO], [20ºC] = 111 d LUFA 6S: DT50 soil, [SFO], [20ºC] = 152 d	

Environmental fate			
		geometric mean (20°C): DT50 soil = 131.6 d Mineralisation: 14.5% AR in LUFA 2.2, 13.4% AR in RefeSol 02-A, 13.0% AR in LUFA 2.3 and 10.9% AR in LUFA 6S. NER: 5.9% AR (RefeSol 02-A), 10.6% AR (LUFA 2.2), 2.4% AR (LUFA 2.3) and 7.1% AR (LUFA 6S). Relevant metabolites: Unknown 1 and Unknow 2	

Study type	Test protocol	Endpoint/Result	Remarks
Algae, growth inhibition test/ *Pseudokirchneriella subcapitata*	OECD 201	72h ErC50 > 11.2 mg/L 72h ErC10 = 9.74 mg/L	
Daphnia sp. immobilisation	OECD 202	48h EC50= 1.67 µg/L 48h EC10= 0.590 µg/L	m concentration
Daphnia magna, reproduction	OECD 211	21d NOEC = 0.173 µg/L	Tier B
Fish, acute toxicity/*O. Mykiss*	OECD 203	96h EC50= 0.503 mg/L 96h EC10= 0.440 mg/L	
Sediment dweling organisms (*C. riparius*)	OECD 218	28 d EC50 = 2.931 µg/kg dry sediment (mm) EC10 = 0.633 µg/kg	
Soil microorganisms: Nitrogen transformation test (28 days)	OECD 216	≤ 25% of control	Trigger value: 25% deviation from the control
Terrestrial Plants, growth test	OECD 208	*Lolium perenne* (most sensitive) EC50 = 28.9 mg/kg (fresh weight)	6 species: *Brassica napus,* *Glycine max,* *Cucumis sativus,* *Solanum lycopersicum,* *Lolium perene,* *Allium cepa*
Earthworm reproduction	OECD 222	Mortality: NOEC = 16 mg/kg dw Reproduction: NOEC = 16 mg/kg dw	
Dung fly larvae/*Scathophaga stercoraria L.*	OECD 228	Emergence EC50 = 355 µg/kg dw = 42.36 µg/kg fw**	

		Development EC50 = n.d.[1]	
Dung beetle larvae/*Aphodius constans*	OECD 122	Mortality 35 d EC50 = 970 µg/kg dw = 325.9 µg/kg fw***	
Bioaccumulation in fish/*O. mykiss*	OECD 305	BCF = 1.09 L/kg	

[1]It was not possible to determine the EC50 as effects were observed on the developmental rate at all concentrations.
***The EC50 value reported in the Dung fly larvae study of 355 µg/kg dwt has been converted to wet weight considering a relation between dung dwt and wwt of 1:8.831 due to the different water content of the bovine dung used in the toxicity tests.*
****The EC50 value reported in the Dung beetle larvae study of 970 µg/kg dwt has been converted to wet weight considering a relation between dung dwt and wwt of 1:2.976 due to the different water content of the bovine dung used in the toxicity tests.*

Risk characterisation

The Predicted Environmental Concentration (PEC) for each compartment was calculated in accordance with VICH guideline GL6 and the CVMP guideline on the Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-Rev.1)

Using the assessment factors (AF) in these VICH guidelines, predicted no effect concentrations (PNEC) were calculated and compared with the PEC values. This results in a risk quotient (RQ) for each compartment as follows:

Compartment	PNEC	PEC	RQ
Surface water (run off)	0.0173 µg/L	0.011 µg/L	**0.63**
Surface water (direct excrection)	0.0173 µg/L	0.52 µg/L	**30.06**
Surface water (direct excrection) – refined Aquatic invertebrate	0.0173 µg/L	0.098 µg/L	**5.66**
Surface water (direct excrection) – refined Sediment	0.273 µg/L	1.95 µg/L	**7.14**
Groundwater	0.000167 µg/L	0.034 µg/L	203.6
Groundwater – refined	0.0014 µg/L	0.0000001 µg/L	0.00007
soil microorganisms: Nitrogen transformation test	<>25% difference in N transformation	NA	NA
soil	289 (terrestrial plants)	2.45 µg/Kg	0.008
dung	0.424	350 µg/kg	**825.5**

The risk characterisation resulted in risk quotients (RQs) below 1 for the groundwater and soil compartments indicating that the product will not pose a risk to those compartments when used as recommended.

The results of the assessment for the surface water and dung compartments indicate that a risk for the environment is indicated and that the following risk mitigation measures are required for this VMP:

3.5 Special precautions for use

Special precautions for the protection of the environment:

The use of the veterinary medicinal product poses a risk to dung fauna and aquatic and sediment organisms. Like other macrocyclic lactones, eprinomectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of eprinomectin may take place over a period of several weeks. Faeces containing eprinomectin excreted onto pasture by treated 5 animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.
Based on the excretion profile of eprinomectin when administered as the pour-on formulation, treated animals should not have access to watercourses during the first 7 days after treatment.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding repeated use of eprinomectin (and products of the same anthelmintic class). The product should be used only according to the summary of product characteristics instructions.

The following information on environmental properties needs to be included in the product literature:

Environmental properties

Eprinomectin is toxic to aquatic organisms, is very persistent in soils and may accumulate in sediments.

PBT assessment

PBT-assessment			
Parameter	**Result relevant for conclusion**		**Conclusion**
Bioaccumulation	BCF	1.09 L/kg	not B
Persistence	$DT_{50,\ compartment,\ 12\ °C}$	288.9	vP
Toxicity	NOEC	0.0001763 mg/L	T
PBT-statement:	The compound is not considered as PBT nor vPvB		

3.B. Residues documentation

No residue depletion studies were conducted because bioequivalence with the reference product has been demonstrated. Therefore, the same withdrawal periods authorised for the reference product can be applied.

Maximum Residue Limits

Eprinomectin is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	**Marker residue**	**Animal species**	**MRLs**	**Target tissues**	**Therapeutic Classification**
Eprinomectin	Eprinomectin B1a	All ruminants, *equidae*	50 µg/kg 250 µg/kg 1500 µg/kg 300 µg/kg	Muscle Fat Liver Kidney	Antiparasitic agents/ Agents acting against endo- and ectoparasites

			20 µg/kg	Milk	
		Fin fish	50 µg/kg	Muscle and skin in natural proportions	
		Rabbits	50 µg/kg 250 µg/kg 1500 µg/kg 300 µg/kg	Muscle Fat Liver Kidney	

Withdrawal Periods

Based on the data provided above, the following withdrawal periods are justified:

Cattle:
Meat and offal: 15 days.
Milk: Zero hours.

Sheep:
Meat and offal: 2 days
Milk: Zero hours

Goats:
Meat and offal: 1 day
Milk: Zero hours

4. EFFICACY DOCUMENTATION

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, efficacy studies are not required. The efficacy claims for this VMP are equivalent to those of the reference VMP.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

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

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. The current SPC is available in the Union Product Database (UPD).

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 VMP.

None.