

IPAR



**Publicly Available Assessment Report for a
Veterinary Medicinal Product**

Pereprin 5 mg/ml pour on solution for cattle, sheep and goats

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Pereprin 5 mg/ml pour on solution for cattle, sheep and goats
Active substance(s)	Eprinomectin
Applicant	Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerpen, Belgium
Legal basis of application	Article 18 of Regulation 2019/6 (generic veterinary medicinal product)
Date of completion of procedure	
Target species	Cattle (dairy cattle and for meat production), sheep, goats
Indication for use	<p>For treatment of infestations with the following parasites:</p> <p>Cattle:</p> <p>Gastrointestinal roundworms (adults and fourth-stage larvae)</p> <p><i>Ostertagia</i> spp. <i>Ostertagia lyrata</i> (adults only) <i>Ostertagia ostertagi</i> (including inhibited L4) <i>Cooperia</i> spp. (including inhibited L4) <i>Cooperia oncophora</i> <i>Cooperia pectinata</i> <i>Cooperia punctata</i> <i>Cooperia surnabada</i> <i>Haemonchus placei</i> <i>Trichostrongylus</i> spp. <i>Trichostrongylus axei</i> <i>Trichostrongylus colubriformis</i> <i>Bunostomum phlebotomum</i> <i>Nematodirus helvetianus</i> <i>Oesophagostomum</i> spp. (adults only) <i>Oesophagostomum radiatum</i> <i>Trichuris</i> spp. (adults only)</p> <p>Lungworms</p> <p><i>Dictyocaulus viviparus</i> (adults and L4)</p> <p>Warbles (parasitic stages)</p> <p><i>Hypoderma bovis</i> <i>H. lineatum</i></p> <p>Mange Mites</p> <p><i>Chorioptes bovis</i> <i>Sarcoptes scabiei</i> var. <i>bovis</i></p> <p>Lice</p> <p><i>Damalinea bovis</i> (biting lice) <i>Linognathus vituli</i> (sucking lice) <i>Haematopinus eurytarnus</i> (sucking lice) <i>Solenopotes capillatus</i> (sucking lice)</p> <p>Horn flies</p> <p><i>Haematobia irritans</i></p> <p>Prolonged Activity</p> <p>The veterinary medicinal product, applied as recommended, effectively controls reinfections with <i>Ostertagia</i> spp. (including <i>O. ostertagi</i> and <i>O. lyrata</i>), <i>Cooperia</i> spp. (including <i>C. oncophora</i>, <i>C. punctata</i> and <i>C. surnabada</i>), <i>Nematodirus helvetianus</i>, <i>Oesophagostomum radiatum</i> and <i>Dictyocaulus viviparus</i> for up to 28 days after treatment and <i>Haemonchus placei</i> and <i>Trichostrongylus</i> spp. (including <i>T. axei</i> and <i>T. colubriformis</i>) for up to 21 days after treatment. The</p>

	<p>veterinary medicinal product controls <i>Haematobia irritans</i> (horn flies) for at least 7 days after treatment. For the 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.</p> <p>Sheep:</p> <p>Gastrointestinal roundworms (adults) <i>Teladorsagia circumcincta (pinnata/trifurcata)</i> <i>Haemonchus contortus</i> <i>Trichostrongylus axei</i> <i>Trichostrongylus colubriformis</i> <i>Nematodirus battus</i> <i>Cooperia curticei</i> <i>Chabertia ovina</i> <i>Oesophagostomum venulosum</i></p> <p>Lungworm (adult) <i>Dictyocaulus filaria</i></p> <p>Goats:</p> <p>Gastrointestinal roundworms (adult) <i>Teladorsagia circumcincta (pinnata/trifurcata)</i> <i>Haemonchus contortus</i> <i>Trichostrongylus axei</i> <i>Trichostrongylus colubriformis</i> <i>Nematodirus battus</i> <i>Cooperia curticei</i> <i>Oesophagotomum venulosum</i></p> <p>Lungworm (adult) <i>Dictyocaulus filaria</i></p>
ATC vet code	QP54AA04
Concerned Member States	AT, BE, BG, CZ, CY, DE, DK, EE, EL, ES, FR, HR, HU, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK(NI)

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (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 relevant articles of Regulation (EU) 2019/6. 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.

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 5 mg/ml of eprinomectin and the excipients butylhydroxytoluene all-rac-alpha-tocopherol and propylene glycol dicaprylocaprate. The containers are white, high-density polyethylene bottles and white high-density polyethylene backpack bottles closed with black screw closure made of polypropylene with a polyethylene-lined sealing disk (wadding) for induction sealing inside. Each bottle is packed in a box containing a polypropylene spigot cap. 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.

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)

This is a generic application according to Article 18 of Regulation (EU) 2019/6. Eprinex Multi 5 mg/ml pour-on solution for cattle, sheep and goats (VPA 10454/034/001 – Boehringer Ingelheim Vetmedica GmbH) is the cited reference product for the purpose of demonstrating bioequivalence. The reference VMP was first authorised in the RMS in December 2016 in accordance with Article 13(a) of Directive 2001/82/EC as amended (a bibliographic application).

However, Eprinex 0.5% w/v Pour-on Solution for Beef and Dairy Cattle (VPA10454/033/001, authorised 14/08/1998) is the cited reference product for the purpose of applying the rules of the protection of technical documentation. Eprinex 0.5% pour-on was authorised based on submission of a full dossier in accordance with Article 12(3) of Directive 2001/82/EC. Eprinex Multi is considered to be included under the '*same marketing authorisation*' as Eprinex 0.5% w/v Pour-on Solution for Beef and Dairy Cattle.

The safety aspects of this product are accepted as being the same as those of the reference product(s).

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

III. SAFETY ASSESSMENT**III.A Safety Testing****Pharmacological Studies**

In relation to bioequivalence, a waiver from the requirement to provide *in vivo* bioequivalence data was accepted based on compliance with the conditions set out in section 7.1 b) of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4) for products intended for systemically acting topical administration. The candidate product has the same active substance in the same concentration, same pharmaceutical form and qualitatively the same excipients as that of reference product, and it has been adequately justified that any difference(s) in the concentration of excipients will have no influence on the rate and/or extent of absorption of the active substance.

User Safety

It is accepted that risk posed to a user by the candidate product will not differ from that posed by the approved reference product. The following warnings and precautions as listed on the product literature are considered adequate to ensure safety to users of the product:

"This veterinary medicinal product may be irritating to skin and eyes and may cause hypersensitivity reactions.

People with known hypersensitivity to eprinomectin or butylhydroxytoluene and propylene glycol dicaprylocaprate should avoid contact with the veterinary medicinal product.

Eprinomectin can be transferred to breast milk. Therefore, breast-feeding users should handle the veterinary medicinal product with great care.

Personal protective equipment consisting of rubber gloves, boots and waterproof coat should be worn when handling the veterinary medicinal product.

Should clothing become contaminated, remove as soon as possible and launder before re-use.

Avoid contact with eyes and skin. In case of accidental spillage on skin, wash the affected area immediately with soap and water. In case of accidental eye contact, flush eyes immediately with plenty of clean water. Should irritation persist, seek medical advice and show the package leaflet or the label to the physician.

Do not ingest. In case of accidental ingestion, rinse out mouth thoroughly with water, seek medical advice immediately and show the package leaflet or label to the physician.

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

Wash hands after use."

Environmental Risk Assessment

The applicant waives the need for an environmental risk assessment based on the CVMP Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6 (EMA/CVMP/ERA/622045/2020). During pre-submission meetings with the RMS, it was agreed that Eprinex Multi 5 mg/ml pour-on solution for cattle, sheep and goats can be considered the 'same marketing authorisation' as Eprinex 0.5% w/v Pour-on Solution for Beef and Dairy Cattle (VPA10454/033/001, authorised 14/08/1998).

A similar veterinary medicinal product, Eprecis 5 mg/ml pour-on solution for cattle, sheep and goats (Ceva Sante Animale), has been authorised in the community since September 2015. On this basis, this approach is considered acceptable. Furthermore, the reference product for purposes of demonstrating bioequivalence (Eprinex Multi) was authorised in 2016; therefore, the risk to the environment was evaluated according to current requirements.

Conclusion

The RMS concludes that the RMMs that apply to the reference product should also be applied to the candidate product. It is accepted that the candidate formulation will not present an unacceptable risk for the environment when handled, used, stored, and disposed of in accordance with the recommendations included in the proposed SPC.

III.B Residues Documentation**Residue Studies**

No residue depletion studies were conducted in support of this application, as bioequivalence with the reference product has been demonstrated.

MRLs

the active substance, eprinomectin (marker residue Eprinomectin B1a), is listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 with the following MRLs for all ruminants:

50 µg/kg Muscle

250 µg/kg Fat

1500 µg/kg Liver

300 µg/kg Kidney

20 µg/kg Milk

The MRL status for each of the excipients of 'Pereprin 5 mg/ml pour on solution for cattle, sheep and goats' is indicated in the following table:

Qualitative composition of excipients and other constituents	MRL status
Butylhydroxytoluene (E321)	Table 1, no MRL required
Propylene glycol dicaprylocaprate (E 477)	Table 1, no MRL required
All-rac-alpha-tocopherol (E307)	Table 1, no MRL required

The excipients are approved as additives in foodstuffs for human consumption and are therefore allowed substances for which Table I of the Annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required.

Withdrawal Periods

The withdrawal periods proposed by the applicant are the same as those for the authorised reference product, *Eprinex Multi 5 mg/ml pour-on solution for cattle, sheep and goats*:

Meat and offal:

Cattle: 15 days.

Sheep: 2 days.

Goats: 1 day.

Milk:

Cattle, sheep, goats: zero hours.

IV. CLINICAL ASSESSMENT

This is a generic application, submitted in accordance with Article 18 of Regulation (EU) 2019/6. According to Article 18, an application for a marketing authorisation for a generic veterinary medicinal product does not need to contain the documentation on efficacy if the conditions for a generic veterinary medicinal product are met.

A waiver from the requirement to provide *in vivo* bioequivalence data is claimed based on compliance with the conditions set out in section 7.1b) of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4), for products intended for systemically acting topical administration. This biowaiver can be accepted, considering that the candidate product has the same active substance in the same concentration, same pharmaceutical form and the same excipients as that of reference product, and it has been 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 such, efficacy studies are not required, and the efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies (pharmaceuticals only)

Pharmacological Studies

The applicant has proposed inclusion of the same information in sections 4.2 and 4.3 of the SPC 'Pharmacodynamics' and 'Pharmacokinetics' as that contained in the corresponding sections of the SPC of the approved reference product, which is considered acceptable.

Tolerance in the Target Species of Animals

It is accepted that the target animal safety profile of the candidate product will not differ from that of the reference product. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

The applicant has provided a summary of published literature concerning reported resistance to eprinomectin. The SPC for the candidate product contains similar warnings concerning the development of resistance as are included in the SPC of the reference product, and these have been suitably updated where necessary.

IV.B Clinical Studies

No clinical studies have been provided in support of this application; it is accepted that 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.