IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

PRODUCT SUMMARY

EU Procedure number	IE/V/0517/001/DC
Name, strength and pharmaceutical form	Trovex 1mg/ml suspension for injection
Active substance(s)	Dexamethasone isonicotinate
Applicant	Emdoka bvba John Lijsenstraat 16 B-2321 Hoogstraten Belgium
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	28/07/2021
Target species	Cats, cattle, dogs, pigs, horses
Indication for use	Horses, cattle, pigs, dogs and cats: Treatment of inflammatory skin conditions, diseases of the locomotor system and diseases of the respiratory system. Cattle: Treatment of ketosis (acetonaemia).
ATCvet code	QH02AB02
Concerned Member States	AT, BE, BG, CZ, DE,DK, EE, EL, FR, FI, HR, HU, IT, LU, NL, PL, PT, RO, SI, SK, UK(NI)

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 reactions observed are indicated in the SPC.
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 1 mg/ml of dexamethasone isonicotinate. The product includes the excipients: methyl parahydroxybenzoate, propyl parahydroxybenzoate, sodium chloride, polysorbate 80, and water for injections.

The product is packaged in amber, glass multidose vials containing 50 ml of product, sealed with a grey siliconized bromobutyl rubber stopper and aluminium cap. Each vial is packaged in a cardboard box.
The presence of preservatives 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, dexamethasone isonicotinate, is an established active substance described in the European Pharmacopoeia. 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.

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)

The application was made in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application). The reference product cited by the applicant is Voren Suspension for Injection 1mg/ml (VPA10454/025/001, Boehringer Ingelheim Vetmedica GmbH) which was first authorised in the RMS on 01/10/1989 in accordance with a full application dossier. The reference product has been authorised for in excess of ten years and can therefore be accepted as a valid reference product in this generic application.

The applicant claims exemption from the requirement to conduct bioequivalence studies in accordance with paragraph 7.1(d) of Guideline (EMEA/CVMP/016/2000-Rev.3) which permits exemption where:

'*The formulations are identical (identical active substances and excipients as well as physicochemical properties [e.g. identical concentration, dissolution profile, crystalline form, pharmaceutical form and particular size distribution with identical manufacturing process]).*'

Based on the argumentation and quality data provided by the applicant, the claimed exemption is accepted. Studies have been conducted to determine the composition of the generic product compared with that of the reference product and it was accepted that the results confirm that the products are comparable in terms of composition and physicochemical properties. Hence bioequivalence can be assumed and *in vivo* bioequivalence studies are not required.
The safety aspects of this product are considered to be comparable to that of the reference product.
Warnings and precautions as listed on the product literature include those of the reference product and are adequate to ensure safety of the product to users, the consumers of foodstuffs from treated animals and for the environment.

III.A Safety Testing
Pharmacological Studies
As this is a generic application according to Article 13, and bioequivalence with a reference product has been accepted, results of pharmacological tests are not required.

Toxicological Studies
As this is a generic application according to Article 13, and bioequivalence with a reference product has been accepted, results of toxicological tests are not required.

User Safety
No user safety assessment was provided. Based upon comparability of the generic and reference product, it was accepted that no difference in terms of safety for the user is anticipated between the generic and reference products. Further, the product is intended to be administered to the same target species, using the same route of administration at the same dose rate as already approved for the reference product.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:
This product contains dexamethasone and parahydroxybenzoates (parabens), which can cause allergic reactions in some people.
People with known hypersensitivity to dexamethasone or to any of the excipients should avoid contact with the veterinary medicinal product.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Dexamethasone may affect fertility or the unborn child. Pregnant women should not handle this veterinary medicinal product.
This product is a skin and eye irritant. Avoid contact with skin and eyes. In the event of accidental eye or skin contact, wash/irrigate the area with clean running water. Seek medical attention if irritation persists.
Wash hands after use.

It was concluded that the product will not present an unacceptable risk for the user when handled, used, stored and disposed of in accordance with the recommendations included in the SPC.

Environmental Risk Assessment

Phase I
The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will be used to treat a small number of animals in a herd only.

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.

III.B Residues Documentation

Residue Studies
No residue depletion studies were conducted because bioequivalence with the reference product was considered to be supported and the formulation of the generic and reference products were considered to be sufficiently similar to permit extrapolation of withdrawal periods.

MRLs

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

	Bovine	**Porcine**	**Equidae**
Muscle	0.75 µg/kg	0.75 µg/kg	0.75 µg/kg
Liver	2 µg/kg	2 µg/kg	2 µg/kg
Kidney	0.75 µg/kg	0.75 µg/kg	0.75 µg/kg
Milk	0.3 µg/kg	-	-

Withdrawal Periods

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

Cattle:
Meat and offal: 55 days
Milk: 60 hours

Pigs:
Meat and offal: 55 days.

Horses:
Meat and offal: 63 days.
Milk: Not authorised for use in horses producing milk for human consumption.

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13, and bioequivalence with a reference product has been accepted, efficacy studies are not required. The efficacy claims for this product are 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 generic 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.