College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Profexx 50 mg/ml solution for injection for cattle

PRODUCT SUMMARY

EU procedure number	NL/V/0409/001
Name, strength and pharmaceutical form	Profexx 50 mg/ml solution for injection for cattle
Applicant	Alfasan Nederland BV Kuipersweg 9 3449 JA Woerden The Netherlands
Active substance(s)	Carprofen
ATC vetcode	QM01AE91
Target species	Cattle
Indication for use	An adjunct to antimicrobial therapy to reduce clinical signs in acute infectious respiratory disease and acute mastitis in cattle

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*	Generic application in accordance with Article 18 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Rimadyl Cattle 50 mg/ml oplossing voor injectie
Marketing authorisation holder	Zoetis B.V.
MS where the RP is or has been authorised	NL
Marketing authorisation number EU procedure number	REG NL 10078
Date of authorisation	July 2003
Date of completion of the original decentralised procedure	20 December 2023
Date veterinary medicinal product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK(NI)
Concerned Member States for subsequent recognition procedure	
Withdrawn CMS during original decentralised procedure	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)

A. Product description

The VMP contains Carprofen (50 mg/mL). The excipients are Benzyl alcohol, ethanol 96%, Macrogol 400, Poloxamer 188, Ethanolamine (for pH control) and Water for injections

The container/closure system is a sterile and multi-dose container: a 50, 100 mL and 250 mL sized, colourless, type II glass vial, which is closed by a grey type I rubber stopper and sealed by an aluminium cap.

The choice of the formulation and presence of preservatives are justified. The type of preservatives (Benzyl alcohol and ethanol 96%) and their concentrations are the same as per reference product.

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

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 two batches of the product have been presented in accordance with the relevant European guidelines

The product is manufactured including standard manufacturing techniques. The proposed non-sterilising filter is acceptable. The applicant has demonstrated that osmolality is not a critical quality attribute for the proposed drug product, and that osmolality remains well controlled during the manufacturing and storage.

C. Production and control of starting materials

The active substance is Carprofen, an active substance described in the European Veterinary Pharmacopoeia, the USP and the British 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 have been provided.

The excipients are in conformity with the Ph.Eur. requirements. Their specifications are acceptable.

The proposed container closure system is justified. The information provided for the container closure system is accepted.

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

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 VMP.

The analytical methods of the drug product specification have been adequately described and validated. Compliance with the specification of the finished product has been demonstrated on two batches of the finished product. The elemental impurities RA is acceptable.

F. Stability tests

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data have been provided on two batches of the proposed veterinary medicinal product for 18 months under long-term stability condition and for 6 months under accelerated stability condition. Also the stability results of the inverted product have been provided up to six months under long-term stability condition. All results are within the proposed specification limits. The proposed shelf-life of 30 months with a special storage condition is acceptable. The proposed storage condition is acceptable as the product has been found to be photosensitive.

The claim of a 28 days in-use stability after first opening is based on the demonstration of stability for two batches broached and stored 28 days at +30°C at the beginning of shelf life for up to six months. The applicant commits to repeat the in-use stability test when the end of the shelf life is approaching, as per NfG on in-use stability testing of veterinary medicinal products. The preservative effect of Benzyl alcohol and ethanol 96% has been demonstrated up to 28 days

G. Other information

None.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and essential similarity to a reference VMP has been demonstrated, results of safety tests are not required.

The safety aspects of this VMP are identical to the reference VMP.

Warnings and precautions as listed on the product literature are the same as those of the reference VMP and supplemented with additional statements, based on increased knowledge and the current state of science. This information is considered adequate to ensure safety of the product to users / the environment / consumers.

A. Safety tests

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.

The same user safety warnings approved for the reference product were proposed to be applied to the VMP.

Additionally, as hypersensitivity reactions due to the presence of active substance carprofen or excipients benzyl alcohol or macrogol cannot be excluded, the user should be warned and the hazard should be specified.

A risk characterization for accidental self-injection was performed. Gastrointestinal effects, such as nausea, diarrhea are more common side effects, but also peptic ulceration and gastrointestinal bleeding have been reported in humans.
Although it can be questioned whether serious adverse effects would occur after single exposure, it is agreed that adverse effects cannot be fully excluded after accidental self-injection. Therefore, it is justified to have warnings in place for accidental self-injection.

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 environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

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 flock or herd.

B. Residues documentation

Residue tests

No residue depletion studies were conducted.

The Active substance and excipient are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active Substance	Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Therapeutic Classification
Carprofen	Sum of carprofen and carprofen glucuronide conjugate	Bovine, *Equidae*	500 µg/kg 1 000 µg/kg 1 000 µg/kg 1 000 µg/kg	Muscle Fat Liver Kidney	NO ENTRY	Anti-inflammatory agents/Non-steroidal anti-inflammatory agents
	NOT APPLICABLE	Bovine	No MRL required for milk	NOT APPLICABLE		
Benzyl Alcohol	NOT APPLICABLE	All food producing species	No MRL required	For use as excipient	NO ENTRY	NO ENTRY
Poloxamer	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	NO ENTRY	NO ENTRY
Ethanol	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	For use as excipient.	NO ENTRY
Polyethylene glycols (molecular weight ranging from 200 to 10 000)	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	NO ENTRY	NO ENTRY

Withdrawal Periods

Based on the data provided above, the following withdrawal period are justified, in line with the reference VMP:

Meat and offal: 21 days

Milk: zero hours.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and essential similarity to 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