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AGENCE NATIONALE DU
MEDICAMENT VETERINAIRE

FRENCH AGENCY FOR FOOD, ENVIRONNEMENTAL AND OCCUPATIONAL HEALTH SAFETY

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

14 RUE CLAUDE BOURGELAT – PARC D'ACTIVITES DE LA GRANDE MARCHE JAVENE – CS 70611 – 35306 FOUGERES

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dophacyl Avi (Avi-Cyl) powder for use in drinking water for chickens

15 November 2024

PRODUCT SUMMARY

EU procedure number	FR/V/0486/001/DC
Name, strength and pharmaceutical form	Dophacyl Avi, 1000 mg/g powder for use in drinking water for chickens (AT, BE, BG, CY, DE, EE, EL, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SK) Dophacyl Avi powder for use in drinking water for chickens (FR) Avi-Cyl, 1000 mg/g powder for use in drinking water for chickens (HR)
Applicant	Dopharma Research B.V. Zalmweg 24 Raamsdonksveer Noord-Brabant 4941 VX Netherlands
Active substance(s)	Salicylic acid (as sodium salicylate)
ATC vetcode	QN02BA04
Target species	Chickens
Indication for use	Symptomatic treatment of febrile conditions and mild to moderate pain.

Dophacyl Avi powder for use in drinking water for chickens	FR/V/0486/001/DC
Dopharma Research B.V.	DCP
Publicly available assessment report	

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*	Article 19(1) Hybrid application (Règlement (EU) 2019/6).
Reference product (RP)	Aspirine 50 Coophavet
Marketing authorisation holder	Dopharma France
MS where the RP is or has been authorised	France
Marketing authorisation number EU procedure number	FR/V/5748318 2/1992
Date of authorisation	20/07/1992
Proprietary data have been submitted for the following part of the dossier	Tolerance in the target species, withdrawal periods
Date of completion of the original decentralised procedure	02/10/2024
Concerned Member States for original procedure	AT, BE, BG, CY, DE, EE, EL, FR, HR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SK.
Concerned Member States for subsequent recognition procedure	Not applicable

*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

A. Product description

The VMP contains sodium salicylate at a concentration of 1000 mg/g. There is no excipient in the formulation.

The container and closure system are described in the relevant section of the SPC.

The choice of the formulation is justified.

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 the VMP have been presented in accordance with the relevant European guidelines.

C. Production and control of starting materials

The active substance is sodium salicylate, an established active substance described in the European Pharmacopeia. 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.

One supplier is supported by scientific data and a certificate of suitability issued by the EDQM has been provided for the other one.

There are no substance within the scope of the TSE Guideline present or used in the manufacture of this VMP.

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

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.

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.

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 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.

G. Other information

Not applicable

3. SAFETY DOCUMENTATION (safety and residues tests)

A. Safety tests

This is a hybrid application according to Article 19 of Regulation (EC) 2019/6 because there is a change in the active substance of the hybrid veterinary medicinal product compared to the reference veterinary medicinal product.
The active substance of the reference product ASPIRINE 50 COOPHAVET is acetyl salicylic acid; the active substance of Dophacyl Avi is sodium salicylate. Both substances belong to the group of the salicylates only differing in the presence of an acetyl group for acetyl salicylic acid.
Bioequivalence was demonstrated between Dophacyl Avi and the reference product after administration of both sodium salicylate and acetyl salicylic acid (see chapter 4.A).

Pharmacological studies

See Part 4.A.

Toxicological studies

This is an application submitted in accordance with article 19(1) of Regulation (EU) 2019/6, a so called hybrid application and bioequivalence with the reference product has been established (see part 4 of the dossier), therefore, results of toxicological studies are not required.

User safety

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

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 active substance is a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment.

A phase II is not required.

B. Residues documentation

Residue tests

Two original pivotal residue depletion studies were provided. Validation of the analytical method used were provided. It can be concluded that the determination of sodium salicylate residue levels in all matrices were robust and yielded reliable results.

The withdrawal period in meat and offal was established based upon the alternative method in muscle with the addition of a safety span of 30% i.e. two days. The product is not for use in birds producing or intended to produce eggs for human consumption.

Maximum Residue Limits

Prior to the application for marketing authorisation of the veterinary medicinal product, the applicant submitted an application for the extension of the MRL with the result that Sodium salicylate is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmaco-logically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions	Therapeutic classification
Sodium salicylate	salicylic acid	Poultry other than turkey	250 µg/kg 500 µg/kg 1000 µg/kg 250 µg/kg	Muscle Liver Kidney Skin and fat in natural proportions	Not for use in animals producing eggs for human consumption.	Anti-inflammatory agents/Non-steroidal anti-inflammatory agents

Withdrawal Periods

Based on the data provided above, a withdrawal period of 2 days for meat in chicken is justified.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

This is a hybrid application according to Article 19 Article 19 of Regulation (EC) 2019/6, which is similar to a reference VMP and rely in part on the results of the appropriate pre-clinical and clinical studies for this reference product, and in part on new data.

A. Pre-Clinical Studies

Pharmacology

The applicant has submitted a study investigating the pharmacokinetics of salicylic acid following intravenous and oral administration of sodium salicylate, along with two *in vivo* bioequivalence studies in the target species, chickens.

Dose determination and confirmation

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated (see above), dose determination and confirmation studies are not required.

Tolerance in the target species of animals

The applicant has performed a GLP study performed according VICH GL43.
In this study, the veterinary medicinal product was administered 10 days at 0, 1x, 5x and 10x the recommended dose via medicated water in chickens weighing 1.16 ± 0.26 kg.
Up to 10 times the recommended therapeutic dose during more than 3 times the maximum duration of use, the candidate product is well tolerated in chickens under the experimental conditions of this study.

B. Clinical trials

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

The results from the target animal safety (TAS) study and from the pivotal residues study show adequate medicated water consumption (comparable to the untreated group), i.e. adequate therapeutic exposure to the active substance has been demonstrated.

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.