Austrian
Federal Office for
Safety in Healthcare
BASG

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Duocylat 1000 mg/g –
Powder for oral solution for calves and pigs

(Former: Asprimax)

AT/V/0004/001/DC

Date: 08/06/2010

Last update: 13/02/2024

Module 1-3 reflect the scientific discussion for the approval of *Asprimax 1000 mg/g – Powder for oral solution for calves and pigs*. The procedure was finalised on 10/05/2010. For information on changes after this date please refer to module 4.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	AT/V/0004/001/DC
Name, strength and pharmaceutical form	Asprimax 1000 mg/g powder for oral solution
Applicant	Chevita Tierarzneimittel Ges.m.b.H. Kaplanstrasse 10 A-4600 Wels
Active substance	Sodium salicylate
ATC Vetcode	QN02BA04
Target species	Calves and Pigs
Indication for use	For use in calves for supportive treatment of pyrexia in acute respiratory disease, in combination with appropriate therapy; and in pigs for the treatment of inflammation in combination with concurrent antibiotic therapy, and to promote recovery of respiration and to reduce coughing in respiratory tract infections with concurrent antibiotic therapy.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) website (www.hma.eu).

MODULE 3

SUMMARY OF ASSESSMENT

Legal basis of original application	Application in accordance with Article 13(3) of Directive 2001/82/EC, as amended (a hybrid application)
Reference medicinal product	NA-salicylate 100% powder for use in drinking water for calves and pigs marketed by Dopharma Research B.V.
Date of completion of the original decentralised procedure	10/05/2010
Concerned Member States for procedure	DE

I. SCIENTIFIC OVERVIEW

Asprimax 1000 mg/g powder for oral solution contains the active substance sodium salicylate. The product is authorised to be used in calves and pigs. The product is indicated for use in calves for supportive treatment of pyrexia in acute respiratory disease, in combination with appropriate therapy; and in pigs for the treatment of inflammation in combination with concurrent antibiotic therapy, and to promote recovery of respiration and to reduce coughing in respiratory tract infections with concurrent antibiotic therapy. In calves the dose rate is 20 mg/kg bodyweight (bw) twice daily for 1 to 3 days. In pigs the dose rate is 35 mg/kg bw/day for 5 days. The route of administration is orally.

This application was made in accordance with Article 13(3) of Directive 2001/82/EC, as amended by 2004/28/EC i.e. hybrid application. The reference product is “Na-salicylat 100%, powder for use in drinking water or in milk for calves and pigs”. The product has the same pharmaceutical form, the same qualitative and quantitative composition as the reference product. Difference compared to the reference product is changes in therapeutic indication. The claim “To promote recovery of the respiration and to reduce coughing in respiratory tract infections with concurrent antibiotic therapy” is not included in the reference product.

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

II. QUALITY ASPECTS

A. Composition

The product contains the active substance sodium salicylate 100 mg/g and no excipient.

The product is presented in 1 kg, 2 kg, 2.5 kg and 5 kg trilaminate bags composed of polyester, aluminium foil and polyethylene.

The particulars of the containers and controls performed are provided and conform to the regulation.

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 from a licensed manufacturing site.

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

C. Control of Starting Materials

The active substance is sodium salicylate, an established active substance which is 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 have been provided.

D. 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.

E. Control on intermediate products

Not applicable.

F. 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 have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

G. Stability

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 product throughout its shelf life when stored under the approved conditions.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

A. Safety Testing

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological studies, and studies of other effects were not required. The safety aspects of this product are identical to the reference product. Nevertheless, the applicant provided published data to describe the toxicological profile of sodium salicylate.

User Safety

The user risk assessment addresses the potential exposure and associated risks and the user warnings in the SPC are considered satisfactory.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessments concluded that the product did not pose an unacceptable risk for the environment.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

B. Residues documentation

The applicant has provided a GLP residue depletion study in pigs.
In this study pigs were treated with the test item via the drinking water at a dose of 22.3 mg sodium salicylate/kg bw twice daily for a total of 10 times. Samples of kidney, liver, muscle and skin with subcutaneous fat were taken at day 1, 3 and 5 after treatment and analyzed by a validated LC-MS/MS method. The results showed that salicylic acid concentrations were above LOQ (50 ng/g) in one kidney sample, and in one liver sample on day 5 after treatment.

No residue depletion studies were conducted in calves because bioequivalence was established with the reference product.

MRLs

According Table 1 of Council Regulation (EEC) No 37/2010 no MRLs are required for sodium salicylate when it is used orally in pigs.

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero days for meat and offal is justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

This is a so called “hybrid application” according to article 13(3) of Directive 2001/82/EC, as amended by Directive 2004/28/EC. The product has the same pharmaceutical form as the reference product, the same qualitative and quantitative composition it can therefore be deemed as identical and bioequivalent to the reference product. Therefore, no clinical trials in calves and in pigs for the claim “treatment of inflammation in combination with concurrent antibiotic therapy” are needed.

A dossier relating to the claim “To promote recovery of the respiration and to reduce coughing in respiratory tract infections with concurrent antibiotic therapy” which is not included in the reference product was provided.

A. Pre-Clinical Studies

Pharmacology

The antiphlogistic activity of salicylates and its underlying mechanisms based on the inhibition of the cyclo-oxygenase enzyme are well known and generally accepted.

Pharmacokinetics

Pharmacokinetics in pigs

The applicant has provided data from the literature and additional three GLP studies. The pivotal results are that salicylic acid is rapidly absorbed after oral administration of sodium salicylate to pigs. Maximal plasma concentrations are attained after about one hour. A zero order plasma elimination phase is followed by a first order elimination phase, with a half-life of about one hour. No accumulation occurs after repeat administration. The excretion occurs mainly via urine as salicylic acid and salicyluric acid.

Pharmacokinetics in calves

This is a so called “hybrid application” according to article 13(3) of Directive 2001/82/EC, as amended by Directive 2004/28/EC. The product has the same pharmaceutical form as the reference product, the same qualitative and quantitative composition it can therefore be deemed as identical to the reference product.
Consequently, the applicant did not provide pharmacokinetics studies in calves.

Tolerance in the Target Species of Animals

Tolerance in pigs

A tolerance study in pigs was provided.

The formula has a large therapeutic range. In dose levels up to 5 times the therapeutic dose the product elicits no clinical signs or adverse effects. The haematological and biochemical parameters are all within the reference range, indicating that no organ damages occur. The warnings in the SPC are appropriate and reflect possible adverse effects related to salicylates.

Tolerance in calves

This is a so called “hybrid application” according to article 13(3) of Directive 2001/82/EC, as amended by Directive 2004/28/EC. The product has the same pharmaceutical form as the reference product, the same qualitative and quantitative composition it can therefore be deemed as identical to the reference product.

Consequently, the applicant did not provide tolerance studies in calves.

B Clinical Studies

This is a so called “hybrid application” according to Article 13(3) of Directive 2001/82/EC as amended by Directive 2004/28/EC. The reference VMP is authorised for the supportive treatment of pyrexia in acute respiratory disease, in combination with appropriate anti-infective therapy, and for administration to pigs for the treatment of inflammation in combination with antibiotic therapy. Consequently, the applicant did not provide clinical studies for these indications.

Proprietary “clinical studies” were presented for the additional therapeutic claim in pigs: “To promote recovery of the respiration and to reduce coughing in respiratory tract infections with concurrent antibiotic therapy.”

Laboratory Trials

In a dose determination study it was shown that in terms of total clinical score, the choice of 35 mg/kg bw is justified.

Field Trials

The clinical efficacy of the formula was described in a field trial. The clinical field study was conducted according the Guideline for the Conduct of Efficacy Studies for Non-Steroidal Anti-inflammatory Drugs (EMEA/CVMP/237/01-FINAL). The dose level of 35 mg/kg bw was efficacious in combination with an antibiotic to improve respiration and cough in pigs with respiratory disease in the first week of treatment, when it was given on 5 consecutive days.

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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

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 Heads of Medicines Agencies (veterinary) website (www.hma.eu).

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.

Significant Changes

Summary of change **(Application number)**	**Approval date**
Change in the invented name of the medicinal product from “Asprimax” to “DUOCYLAT” 1000 mg/g powder for oral solution for calves and pigs. (AT/V/0004/001/IB/002)	03/10/2011
This marketing authorization was renewed unlimited. (AT/V/0004/001/R/001)	19/05/2015
*** No significant changes since ***	