Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED> PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Clindabactin 55 mg Chewable Tablets for Dogs and Cats
Clindabactin 220 mg Chewable Tablets for Dogs
Clindabactin 440 mg Chewable Tablets for Dogs

Date Created: May 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0678/001-003/DC
Name, strength and pharmaceutical form	Clindabactin 55 mg Chewable Tablets for Dogs and Cats Clindabactin 220 mg Chewable Tablets for Dogs Clindabactin 440 mg Chewable Tablets for Dogs
Applicant	Dechra Regulatory BV Handelsweg 25 Bladel 5531 AE The Netherlands
Active substance	Clindamycin Hydrochloride
ATC Vetcode	QJ01FF01
Target species	Cats Dogs
Indication for use	Cats: For the treatment of infected wounds and abscesses, and oral cavity infections including periodontal disease, caused by bacteria susceptible to clindamycin. Dogs: For the treatment of infected wounds and abscesses, and oral cavity infections including periodontal disease, caused by or associated with Staphylococcus spp., Streptococcus spp. (except Streptococcus faecalis), Bacteroides spp., Fusobacterium necrophorum, and Clostridium perfringens susceptible to clindamycin. For the treatment of superficial pyoderma associated with Staphylococcus pseudintermedius susceptible to clindamycin. For the treatment of osteomyelitis, caused by Staphylococcus aureus susceptible to

	clindamycin.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application.	Generic Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure.	13/03/2019
Concerned Member States for original procedure.	Austria, Belgium. Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden.

I. SCIENTIFIC OVERVIEW

Clindabactin 55 mg Chewable Tablets for Dogs and Cats, Clindabactin 220 mg Chewable Tablets for Dogs and Clindabactin 440 mg Chewable Tablets for Dogs; contain 55 mg, 220 mg and 440 mg of clindamycin (as clindamycin hydrochloride) per tablet respectively.

The proposed indications are as follows:
Dogs:

- For the treatment of infected wounds and abscesses, and oral cavity/dental infections, caused by or associated with *Staphylococcus* spp., *Streptococcus* spp. (except *Streptococcus faecalis*), *Bacteroides* spp., *Fusobacterium necrophorum*, and *Clostridium perfringens*.
- For the treatment of superficial pyoderma associated with *Staphylococcus intermedius*.
- For the treatment of osteomyelitis, caused by *Staphylococcus aureus*.

Cats:
For the treatment of infected wounds and abscesses and oral cavity/dental infections, caused by bacteria sensitive to clindamycin.

The applications for all tablet strengths are submitted in accordance with Article 13(3) of Directive 2001/82/EC as amended by 2004/28/EC (as 'hybrid'

applications), due to a change in pharmaceutical strength compared to the reference product. The reference product for all tablet strengths is Antirobe 25 mg (Vm 42058/4003) marketed by Zoetis UK Limited, which was authorised in the UK via a National procedure on 9th June 1989.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] 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. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

Clindabactin chewable tablets for cats and dogs are presented as round, light brown tablets, with a cross-shaped score line on one side, containing 55 mg, 220 mg or 440 mg clindamycin (as clindamycin hydrochloride).
The tablets contain the excipients sodium croscarmellose, starch pregelatinised (maize) cellulose microcrystalline, silica colloidal hydrated, yeast extract, chicken flavour and magnesium stearate.

Clindabactin tablets are presented in aluminium/aluminium blister packs comprising:
Top foil: laminate of polyamide (25 µm) / aluminium (45 µm) / PVC (60 µm)
Bottom foil: aluminium (20 µm)

Each blister strip contains 10 tablets. The blister strips are presented in cartons of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 25 blister strips, i.e. cartons of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or 250 tablets. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are justified.

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

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of weighing, mixing, sieving and blending prior to compressing into tablets. The tablets are then bulk packaged and tested in accordance with the finished product specification.

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

II.C. Control of Starting Materials

The active substance is clindamycin hydrochloride, 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 have been provided.

A Certificate of Suitability was provided for the active substance clindamycin hydrochloride.

The excipients sodium croscarmellose, starch pregelatinised (maize) cellulose microcrystalline, silica colloidal hydrated, and magnesium stearate are described in a pharmacopeia. The excipients yeast extract and chicken flavour are not described in a pharmacopeia and are identified by the manufacturers' in-house product codes and specifications.

The container/closure for the active substance is described in the Certificate of Suitability as double polyethylene bags placed in a cardboard drum.
Polyethylene bags are used for the intermediate storage and transportation of granulates and bulk tablets, the inner bags being clear and the outer bags being black.
The finished product is packed in formed and sealed aluminium/aluminium blister packs.

II.C.4. Substances of Biological Origin

A Certificate of Suitability issued by the EDQM has been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated. The only material of animal origin is the chicken flavour, the ingredients of which are all WU approved feed materials or feed additives.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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 have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, tightness of blister, average mass, uniformity of dosage units, disintegration time, resistance to crushing, identification and assay of clindamycin, degradation, dissolution and microbiological purity.

II.F. 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.

G. Other Information

This veterinary medicinal product does not require any special storage conditions.
Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life of divided tablets after first opening the immediate packaging: 3 days.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Due to the legal base of the applications being generic hybrid applications submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended, pharmacological and toxicological data are not required. A user risk assessment (URA) and environmental risk assessment (ERA) were submitted.

Observations in Humans

The applicant provided data from the SPC for Clindamycin 150 mg Capsules for use in humans as supportive evidence for the URA.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the applicant has identified the primary user risks as hypersensitivity reactions and accidental injection. The applicant has also considered potential local skin and eye irritation from contact between fingers & eyes after handling the tablets. In conclusion, taking into account the formulation of the product and the fact that a warning with respect to hypersensitivity and an advice to wash hands after use is already included in the product information, further risks with regard to the irritating potential (i.e. skin and or eye irritation) of clindamycin are not expected.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.Therefore the following applicant's user recommendations are appropriate:

- Lincosamides (lincomycin, clindamycin, pirlimycin) may cause hypersensitivity (allergy) reactions. People with known hypersensitivity to lincosamides should avoid contact with the veterinary medicinal product.
- Wash hands after handling tablets.
- Accidental ingestion may result in gastro-intestinal effects such as abdominal pain and diarrhoea. Care should be taken to avoid accidental ingestion.
- In order to reduce the risk of accidental ingestion by children, do not take the tablets out of the blister until ready to administer to the animal. Return part-used tablets into the blister and carton and use at the subsequent administration.
- In case of accidental ingestion, particularly by children, seek medical advice immediately and show the package leaflet or the label to the physician.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The applicant worked through the VICH Phase 1 decision tree, the products are intended for the treatment of cats and dogs only and as these are non-food animals, as a result environmental exposure will be low. A Phase II ERA was not required.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

No data was submitted as the applicant stated that in accordance with the legal basis of the applications and given that bioequivalence with the reference product has been established, results of toxicological, pharmacological or clinical tests are not required.

The applicant included a 25 mg chewable tablet in the manufacturing process which was used in the *in vivo* bioequivalence study; however this tablet strength will not be marketed. The applicant conducted an *in-vivo* study in cats comparing this tablet to the reference product Antirobe capsules 25 mg. The applicant claimed exemption from the requirement to conduct further *in vivo* bioequivalence studies in cats with the additional tablet strengths (55 mg, 220 mg, and 440 mg) in accordance with section 7.2 of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2)
The applicant claimed an exemption from the requirement to conduct *in vivo* bioequivalence studies in dogs in accordance with section 7.1(e) of the Guideline (EMA/CVMP/016/00-Rev.2); 'The products are classified as bio-waivers in accordance with principles underlying the BCS. To fulfil the requirements of a bio-waiver the applicant provided additional data to address the solubility and absorption of the active substance, results of an *in vitro* dissolution study with the reference product Antirobe Capsules 25 mg and data pertaining to differences in excipients.

Tolerance in the Target Species

Tolerance studies were not required because this is a hybrid application submitted in accordance with Article 13(3) of the Directive 2001/82/EC as amended, and bioequivalence with the reference product has been established it can be concluded that efficacy and safety data are demonstrated for the candidate product under Article 13 in Directive 2001/82/EC.

Resistance

This is a hybrid application submitted in accordance with Article 13(3) of the Directive 2001/82/EC as amended, bioequivalence with the reference product has been established, results of toxicological, pharmacological or clinical tests are not required. However as the risk of resistance is constantly evolving, data pertaining to the current level of resistance was provided and the SPC updated accordingly, this was in line with the Revised Guideline on the SPC for Antimicrobial Products *(EMEA/CVMP/SAGAM/38441/20015*).

IV.II. Clinical Documentation

The applicant concluded that as bioequivalence between the candidate and reference product has been demonstrated, results of pharmacological, toxicological and clinical tests were not required.

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 of the products is favourable.

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 Product Information Database of the Veterinary Medicines Directorate website.

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The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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