ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Clavudale 50 mg Tablet for Cats and Dogs

(UK, Ireland, France, Austria, Belgium, Czech Republic, Greece, Hungary, Iceland, Luxembourg, Norway, Poland, Portugal, Slovak Republic)

Clavudale 40 mg / 10 mg Tablet for Cats and Dogs

(Germany, Netherlands, Denmark, Spain, Finland, Sweden)

PuAR correct as of 01/08/2018 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0373/001/MR
Name, strength and pharmaceutical form	Clavudale 50 mg Tablet for Cats and Dogs
Applicant	Dechra Limited Dechra House Jamage Industrial Estate Talke Pits Stoke-on-Trent Staffordshire ST7 1XW UK
Active substance(s)	Amoxicillin (as amoxicillin trihydrate) Clavulanic acid (as potassium clavulanate)
ATC Vetcode	QJ01CR02
Target species	Cats and Dogs
Indication for use	For the treatment of bacterial infections susceptible to amoxicillin in combination with clavulanic acid where clinical experience and/or sensitivity testing indicates the product as the drug of choice. Uses include: Skin infections (including deep and superficial pyodermas) associated with Staphylococci and Streptococci; Infections of the oral cavity (mucous membrane) associated with Clostridia, Corynebacteria, Staphylococci, Streptococci, *Bacteroides* spp. and Pasteurellae.; Urinary tract infections associated with Staphylococci, Streptococci, *Escherichia coli* and *Proteus* spp; Respiratory tract infections associated with Staphylococci, Streptococci and Pasteurellae; Gastrointestinal infections associated with *Escherichia coli* and *Proteus* spp.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	02 September 2011
Date product first authorised in the Reference Member State (MRP only)	08 January 2010
Concerned Member States for original procedure	Austria Belgium Czech Republic Denmark Finland France Germany Greece Hungary Iceland Ireland Luxembourg The Netherlands Norway Poland Portugal Slovakia Spain Sweden

I. SCIENTIFIC OVERVIEW

Clavudale 50 mg Tablet for Cats and Dogs is authorised for use in cats and dogs for the treatment of bacterial infections susceptible to amoxicillin in combination with clavulanic acid where clinical experience and/or sensitivity testing indicates the product as the drug of choice. The product is intended for oral administration only and each tablet contains amoxicillin (as amoxicillin trihydrate) 40 mg and clavulanic acid (as potassium clavulanate) 10 mg. The product is packaged in blister packs consisting of orientated polyamide/aluminium/polyvinyl chloride film, heat sealed with aluminium foil (20µm) in strips of 6 tablets. Multiple strips are packed into cartons of twelve or twenty-four tablets. Indications include skin infections (including deep and superficial pyodermas) associated with Staphylococci and Streptococci; infections of the oral cavity (mucous membrane) associated with Clostridia, Corynebacteria, Staphylococci, Streptococci, *Bacteroides* spp. and Pasteurellae.; urinary tract infections associated with Staphylococci, Streptococci, *Escherichia coli* and *Proteus* spp; respiratory tract infections associated with Staphylococci, Streptococci and Pasteurellae; and gastrointestinal infections associated with *Escherichia coli* and *Proteus* spp. The product must not be used in rabbits, guinea pigs, hamsters and gerbils. The product is not be used in animals with known hypersensitivity to penicillin or substances of the ß-lactam group. The dosage rate is 10 mg amoxicillin/2.5 mg clavulanic acid/kg bodyweight twice daily. In refractory cases the dose may be doubled to 20 mg amoxicillin/5 mg clavulanic acid/kg bodyweight twice daily. To ensure a correct dosage, body weight should be determined as accurately as possible to avoid under-dosing.

This application for the mutual recognition of a UK marketing authorisation was submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended by 2004/28/EC. The product was authorised in the UK on 8th January 2010. Bioequivalence is claimed with the reference product Synulox Palatable Tablets, which has been approved in the UK since 1990.

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[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 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.

[1] Summary of Product Characteristics

II. QUALITY ASPECTS

A. Composition

The active substances are amoxicillin (as amoxicillin trihydrate) and clavulanic acid (as potassium clavulanate), and the excipients are erythrosine (E127), silica colloidal anhydrous, magnesium stearate, sodium starch glycolate (Type A) and cellulose microcrystalline.

The product is an established pharmaceutical form and its development has been 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 products have been presented in accordance with the relevant European guidelines.

All ingredients are sieved and blended and the addition of each active substance is adjusted for purity at the expense of microcrystalline cellulose. All components are ground and/or sieved before blending, compacting and tabletting. Tests are performed to examine water content, friability, disintegration, hardness and uniformity of mass. Tablets are marked as appropriate prior to packaging. Validation of the manufacturing process was conducted on three consecutive batches of product. Final specification tests ensure the quality of the products.

C. Control of Starting Materials

The supporting data for amoxicillin trihydrate and potassium clavulanate have been provided in the form of EDQM[2] Certificate of Suitability. It is considered that the manufacturing process is adequately controlled and the active substance specifications have been suitably justified.

There are five excipients used in the formulation and each has been used previously in veterinary medicines. Silica colloidal anhydrous, sodium starch glycolate, magnesium stearate and cellulose microcrystalline, have monographs in the European Pharmacopoeia and each complies with the requirements of the current edition of the Ph. Eur.

The applicant provided raw material specification and certificate of analysis for erythrosine (E127). The certificate of analysis confirms compliance with Directive 95/45/EC. This is considered acceptable.

[2] The European Directorate for the Quality of Medicines & HealthCare.

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

There are no intermediate products.

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.

G. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf-life. The shelf-life of the veterinary medicinal product as packaged for sale is 3 years.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Special precautions for storage:

- Do not store above 25°C.
- Divided tablets should be stored in the blister pack.

Shelf-life:

- Shelf life of the veterinary medicinal product as packaged for sale: 3 years
- Shelf-life after first opening the immediate packaging: 12 hours
- Any divided tablet portions remaining after 12 hours should be discarded.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

As this is a generic application according to Article 13, and bioequivalence with reference products has been demonstrated, results of pharmacological, toxicological, user safety and residues tests were not required. These aspects of the products are identical to the reference products.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which showed that the most likely routes of accidental exposure are oral, dermal and ocular.
The following precautions are listed on the SPC and product literature:

- Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.
- Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.
- Handle this product with great care to avoid exposure, taking all recommended precautions.
- If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.
- Wash hands after use.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guidelines. The assessment ended at Phase I based on use in companion animals only. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

A two-way cross-over bioequivalence study of a single dose of Clavudale 50 mg Tablet for Cats and Dogs as compared to Synulox Palatable Tablets 50 mg was performed. A suitable number of animals were given half or a whole tablet, based on bodyweight. Blood samples were taken at appropriate time points. Statistical analysis demonstrated that the products were bioequivalent.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for these products are equivalent to those of the reference products.

Resistance

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for these products are equivalent to those of the reference products.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for these products are equivalent to those of the reference products.

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.

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.

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

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.

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