Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Clindamycin 600 mg Capsules, hard

clindamycin hydrochloride

PL 20117/0394

Morningside Healthcare Ltd.

LAY SUMMARY

Clindamycin 600 mg Capsules, hard
clindamycin hydrochloride

This is a summary of the Public Assessment Report (PAR) for Clindamycin 600 mg Capsules, hard . It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Clindamycin Capsules in this lay summary for ease of reading.

For practical information about using Clindamycin Capsules, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Clindamycin Capsules and what are they used for?
This application is for a hybrid medicine. This means that the medicine is similar to a reference medicine already authorised, called Dalacin 300mg capsule, albeit with certain differences. In this case, Clindamycin Capsules is a higher dose than the reference product, 600 mg compared to 300 mg (reference product).

Clindamycin Capsules contain clindamycin hydrochloride which is an antibiotic used in the treatment of serious bacterial infections.

How does Clindamycin Capsules work?
The antibiotic in Clindamycin Capsules works by limiting the growth of the bacteria.

How is Clindamycin Capsules used?
The pharmaceutical form of this medicine is capsules and the route of administration is oral (by mouth).

Clindamycin Capsules should always be swallowed whole with a full glass of water. If you have trouble with swallowing medicines, then please ensure you take the capsules in a seated position with a large glass of water whilst leaning slightly forward.

This will help you to swallow the capsules more easily.

Adults and Elderly Patients:
The recommended dose of Clindamycin 600 mg Capsules is (1 capsule) 600 mg capsule every 8 hours.

Clindamycin 600mg Capsules are not suitable for use in children.

For further information on how Clindamycin Capsules is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Clindamycin Capsules have been shown in studies?
Because Clindamycin Capsules is a hybrid medicine, studies in healthy volunteers consist of tests to determine that it is therapeutically equivalent to the reference medicine.

What are the possible side effects of Clindamycin Capsules?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Clindamycin Capsules is a hybrid medicine and is therapeutically equivalent to the reference medicine, its benefits and possible side effects are taken as being the same as the reference medicine.

Why was Clindamycin Capsules approved?
It was concluded that Clindamycin Capsules has been shown to be therapeutically equivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Clindamycin Capsules?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Clindamycin Capsules. The RMP details the important risks of Clindamycin Capsules, how these risks can be minimised, any uncertainties about Clindamycin Capsules (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Clindamycin Capsules:

Summary of safety concerns	
Important identified risks	• Pseudomembranous colitis • Hepatobiliary disorders • Antibiotic resistance • Interaction with vitamin K antagonists (eg. warfarin, acenocoumarol and phenprocoumon • Use in patients with severe renal impairment
Important potential risks	• Neuromuscular junction conduction disorders • Inappropriate dosing in children
Missing information	• Exposure during pregnancy • Exposure during breast-feeding

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Clindamycin Capsules
A marketing authorisation for Clindamycin Capsules was granted in the United Kingdom (UK) on 23 January 2023.

The full PAR for Clindamycin Capsules follows this summary.

This summary was last updated in September 2023.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Clindamycin 600 mg Capsules, hard (PL 20117/0394) could be approved.

Clindamycin is indicated for the treatment of the following infections caused by susceptible anaerobic pathogens:

- Dental infection
- Serious infections caused by anaerobic bacteria, including intra-abdominal infections, and skin and soft tissue infections.

As needed, clindamycin should be administered in conjunction with another antibacterial agent that is active against gram negative aerobic bacteria.

Consideration should be given to the official guidance on the appropriate use of antibacterial agents.

Clindamycin is a lincosamide antibiotic with a primarily bacteriostatic action against Gram-positive aerobes and a wide range of anaerobic bacteria. Lincosamides such as clindamycin bind to the 50S subunit of the bacterial ribosome similarly to macrolides such as erythromycin and inhibit protein synthesis. The action of clindamycin is predominantly bacteriostatic although high concentrations may be slowly bactericidal against sensitive strains. Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

This application was approved under Regulation 52B of The Human Medicines Regulation 2012, as amended (previously Article 10(3) of Directive 2001/83/EC, as amended), claiming to be a hybrid medicinal product of a suitable originator product, Dalacin 300mg capsule that has been licensed for a suitable time, in line with the legal requirements.

Data from a bioequivalence was submitted with this application. This study was conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A national marketing authorisation was granted in the United Kingdom (UK) on 23 January 2023.

The Commission considered the application at its meeting on 30 September 2021.

II QUALITY ASPECTS

II.1 Introduction

The active substance is clindamycin hydrochloride. Each capsule contains clindamycin hydrochloride equivalent to 600 mg of clindamycin. The other ingredients are: lactose monohydrate, maize starch, talc and magnesium stearate.
Capsule shell - (600 mg): gelatin, iron oxide black (E172) and titanium dioxide (E171).
Printing ink - : shellac, titanium dioxide (E171) and propylene glycol (E1520).

The finished product is packaged in blisters of 7, 10, 14, 15, 20, 24, 28, 30, 56, 60, 84, 90, 100, 112 and 120. Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

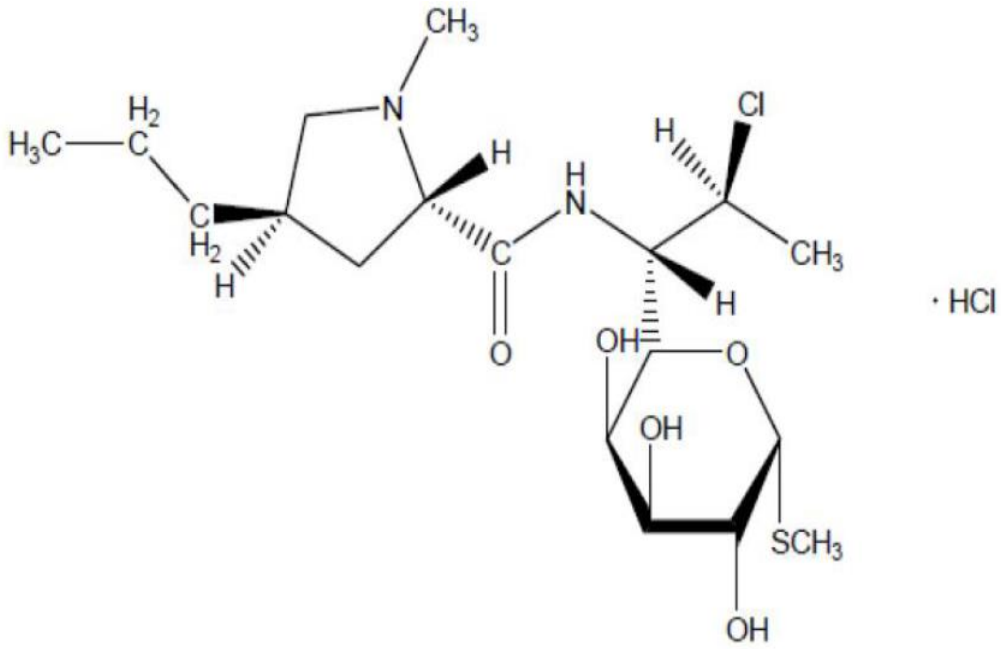
II.2 ACTIVE SUBSTANCE

rINN: Clindamycin hydrochloride

Chemical Name: Methyl 7-chloro-6,7,8-trideoxy-6-[[[(2S,4R)-1- methyl -4-propylpyrrolidin-2-yl]carbonyl]amino]-1- thio-L-threo-α-D-galacto-octopyranoside hydrochloride

Molecular Formula: $C_{18}H_{33}ClN_2O_5S \cdot HCl$

Chemical Structure:



Molecular Weight: 461.5

Appearance: A white or almost white, crystalline powder.

Solubility: Very soluble in water, slightly soluble in ethanol (96 per cent).

Clindamycin hydrochloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution and impurity profiles have been provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

With the exception of gelatin and lactose monohydrate, no excipients of animal or human origin are used in the final products. Certificates of analyses (CoA) and TSE / BSE certificate from each of the manufacturer/supplier of the above excipients were provided.

The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Confirmation has been given that the magnesium stearate used in the capsules is of vegetable origin.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 3 years with the storage conditions “Do not store above 30ºC” is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The grant of a marketing authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of clindamycin hydrochloride is well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology

No new pharmacology data were provided and none were required for this application.

III.3 Pharmacokinetics

No new pharmacokinetic data were provided and none were required for this application.

III.4 Toxicology

No new toxicology data were provided and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As this is a hybrid application of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects

The grant of a marketing authorisation is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

In accordance with the regulatory requirements, data from a bioequivalence study has been submitted with this application. This study was conducted in-line with current Good Clinical Practice (GCP).

IV. 2 Pharmacokinetics

In support of the application, the applicant submitted the following.

An open-label, balanced, randomised, single-dose, two-treatment, two-sequence, two-period, crossover oral bioequivalence study of Clindamycin 600mg capsules (Test) compared with Dalacin® C 150mg Capsules (Reference - 4 capsules x 150mg) in healthy, adult, human male subjects under fasting conditions.

In each study period, after an overnight fast of at least 10 hours subjects were administered with a single dose of the test or reference product. Blood samples were taken pre-dose and up to Clindamycin Capsules 24 post dose, with a washout period of 7 days between the treatment periods.

A summary of the pharmacokinetic results are presented below:

Pharmacokinetic Parameters (Units)	Ln- transformed Geometric Least Squares Mean			90% Confidence Interval (Parametric)	
	Test Product (T)	Reference Product (R)	T/R (%)	Lower	Upper
C_{max} (ng/mL)	9325.0992	9499.4533	98.16	91.51	105.31
AUC_{0-t} (ng.hr/mL)	44924.3357	43225.9677	103.93	97.21	111.11

According to the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

IV.3 Pharmacodynamics
No new pharmacodynamic data have been submitted for this application and none were required.

IV.4 Clinical efficacy
No new efficacy data have been submitted for this application and none were required.

IV.5 Clinical safety
With the exception of the safety data from the bioequivalence study submitted with this application, no new safety data were submitted. The safety data submitted showed that the product was well-tolerated.

IV.6 Risk Management Plan (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects
The grant of a marketing authorisation is recommended for this application.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the guideline on the readability of the label and package leaflet of medicinal products for human use.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified.

Extensive clinical experience with clindamycin hydrochloride is considered to have demonstrated the therapeutic value of the product.

The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory and in line with current guidelines.

In accordance with legal requirements, the current approved versions of the SmPC and PIL for this product is available on the MHRA website.

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**