

IPAR



**Public Assessment Report for a
Medicinal Product for Human Use**

Scientific Discussion

Doxycycline 100 mg hard capsules
Doxycycline hyclate
PA1567/006/002

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

- I. INTRODUCTION
- II. QUALITY ASPECTS
- III. NON-CLINICAL ASPECTS
- IV. CLINICAL ASPECTS
- V. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT
- VI. REVISION DATE
- VII. UPDATE

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Doxycycline 100 mg hard capsules, from Activase Pharmaceuticals Limited on 9th January 2026 for in the treatment of a variety of infections caused by susceptible strains of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

Respiratory tract infections:

Pneumonia and other lower respiratory tract infections due to susceptible strains of *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Moraxellacatarrhali* and other organisms.

Mycoplasma pneumoniae.

Treatment of chronic bronchitis, sinusitis.

Urinary tract infections:

Infections caused by susceptible strains of *Klebsiella* species, *Enterobacter* species, *Escherichia coli*, *Streptococcus faecalis* and other organisms.

Sexually transmitted diseases:

Infections due to *Chlamydia trachomatis* including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal urethritis caused by *Ureaplasma urealyticum* (T-mycoplasma).

Doxycycline is also indicated in infections due to *Calymmatobacteriumgranulomatis*. Doxycycline is an alternative drug in the treatment of gonorrhoea and syphilis.

Since Doxycycline is a member of the tetracycline series of antibiotics, it may be expected to be useful in the treatment of infections which respond to other tetracyclines, such as:

Ophthalmic infections:

Doxycycline capsules are indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence.

Inclusion conjunctivitis may be treated with oral Doxycycline alone or in combination with topical agents.

Rickettsial infections:

Rocky Mountain spotted fever, typhus group, Q fever and *Coxiella endocarditis*.

Other infections:

Psittacosis, brucellosis (in combination with streptomycin), cholera, bubonic plague, louse and tick-borne relapsing fever including stage 1 and stage 2 Lyme disease, leptospirosis, tularaemia glanders, chloroquine-resistant falciparum malaria and acute intestinal amoebiasis (as an adjunct to amoebicides). Infections due to susceptible strains of *Bacteroides* species, *Listeria* species and *Bacillus anthracis*.

Doxycycline is an alternative drug in the treatment of leptospirosis, gas gangrene and tetanus.

Doxycycline is indicated for prophylaxis in the following conditions: Scrub typhus, travellers' diarrhoea (enterotoxigenic *Escherichia coli*), leptospirosis, malaria and cholera.

This application was submitted in accordance with Article 10(1) of Directive 2001/83/EC and is referred to as a 'generic' application. With Ireland as the Reference Member State (RMS) in this decentralised procedure, Activase Pharmaceuticals Limited applied for a marketing authorisation for Doxycycline 100 mg hard capsules in Malta. The reference product was Vibramycin 100 mg capsules, MAH: Pfizer Healthcare Ireland.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie

Name of the product	Doxycycline 100 mg hard capsules
Name(s) of the active substance(s) (INN)	Doxycycline
Pharmacotherapeutic classification (ATC code)	J01AA02
Pharmaceutical form and strength(s)	Hard capsule; 100 mg
Marketing Authorisation Number(s) in Ireland (PA)	PA1567/006/002

Marketing Authorisation Holder	Activase Pharmaceuticals Limited
MRP/DCP No.	IE/H/1288/002/DC
Reference Member State	IE
Concerned Member State	MT

II. QUALITY ASPECTS

II.1. Introduction

This application is for Doxycycline 100 mg hard capsules.

II.2 Drug substance

The active substance is Doxycycline hyclate, an established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

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

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for capsules, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.7 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with EU legislation for use with foodstuffs requirements.

P.8 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical and Pharmaceutical Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Doxycycline 100 mg hard capsules.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Vibramycin capsules on the European market. As the pharmacodynamic, pharmacokinetic and toxicological properties of doxycycline are well known, the applicant has not provided additional nonclinical studies and further studies are not required. The overview provided based on literature review is thus appropriate.

III.2 Ecotoxicity/environmental risk assessment

As doxycycline 50mg and 100mg capsules are generic products, an increased exposure to the environment is not anticipated. Additional ERA studies are not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of doxycycline are well known since it has been marketed for several decades and resulting clinical experience are extensive. As Doxycycline is a widely used, well-known active substance, the applicant has not provided additional non-clinical studies and further studies are not required. Overview based on literature review is, thus, appropriate.

IV. CLINICAL ASPECTS

IV.1 Introduction

Doxycycline is a well-known active substance with established efficacy and tolerability.

The content of the SmPC approved during the decentralised procedure is in accordance with that accepted for the reference product Vibramycin 100 mg capsules marketed by Pfizer Healthcare Ireland.

No bioequivalence study has been submitted to support the application. A BCS-based biowaiver in accordance with ICH M9 has been proposed by the applicant and considered acceptable, based on the following: drug substance is highly soluble/highly permeable (BCS Class I); no excipients included in the formulation which impact on absorption; comparative *in vitro* dissolution between the test and reference product show comparability in dissolution profiles.

IV.2 Pharmacokinetics

No new pharmacokinetic data were submitted. A BCS-based biowaiver in accordance with ICH M9 has been proposed and considered acceptable.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted and none are required for an application of this type.

IV.4 Clinical Efficacy

No new efficacy data were submitted and none are required for an application of this type.

IV.5 Clinical Safety

No new safety data were submitted with this application

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Doxycycline 50mg hard capsules.

Safety specification

Important Identified risks	None
Important potential risks	None
Missing information	None

Pharmacovigilance Plan

Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures.

Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

PSUR

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.
- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.
- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

V. OVERALL CONCLUSIONS

Doxycycline 100 mg hard capsules are generic forms of Vibramycin 100 mg capsules. Vibramycin is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile. A BCS-based biowaiver has been granted in accordance with ICH M9.

The SmPC is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted considered that Doxycycline 100 mg hard capsules has a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

03.12.2030