Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

DOXYCYCLINE 100 MG CAPSULES

PL 20416/0460

UKPAR

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DOXYCYCLINE 100 MG CAPSULES

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted RelonChem Ltd a Marketing Authorisation (licence) for the medicinal product Doxycycline 100 mg Capsules (Product Licence number: 20395/0011). This antibiotic is only available with a prescription.

Doxycycline 100 mg Capsules contain the active ingredient doxycycline hyclate. Doxycycline works by preventing the microorganisms responsible for infection from making the proteins that they need to grow.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Doxycycline 100 mg Capsules outweigh the risks, hence a Marketing Authorisation has been granted.

The Marketing Authorisation underwent a change of ownership procedure from the company RelonChem Ltd (PL 20395/0011) to the company Crescent Pharma Limited (PL 20416/0460) on 19 August 2015.

DOXYCYCLINE 100 MG CAPSULES

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Doxycycline 100 mg Capsules (PL 20395/0011) to RelonChem Ltd on 24 October 2006. This product is a Prescription Only Medicine (POM).

The application was submitted as an abridged informed consent application according to Article 10.1 (a)(i) of EC Directive 2001/83. The cross reference product is Ethypharm Doxycycline 100mg Capsules (PL 12365/0004), held by Ethypharm Labs and granted 11 August 1994.

No new data were submitted, nor was it necessary for this simple application as the data is identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) was generated for it.

The Marketing Authorisation underwent a change of ownership procedure from the company RelonChem Ltd (PL 20395/0011) to the company Crescent Pharma Limited (PL 20416/0460) on 19 August 2015.

PHARMACEUTICAL ASSESSMENT REPORT

INTRODUCTION & BACKGROUND

This is a simple, 'piggy-back' application for Doxycycline 100mg Capsules, submitted under Article 10.1 (a)(i) of Directive 2001/83/EC, as amended, from RelonChem Ltd. The marketing authorisation to which this application cross-refers is PL 12365/0004 for Ethypharm Doxycycline 100mg Capsules, held by Ethypharm Labs, France. This MA was initially granted on 11 August 1994. A letter of informed consent is present. A letter confirming that RelonChem has a copy of the Part II preclinical and clinical data is also provided.

Doxycycline is a broad spectrum antibacterial agent indicated for the treatment of infections caused by chlamydia, rickettsia, brucella and the spirochaete, *Borrelia burgdorferi*. It is also used to treat respiratory and genital mycoplasma infections, acne, destructive periodontal disease, exacerbations of chronic bronchitis and leptospirosis in penicillin hypersensitive patients (BNF, No. 51, March 2006). In particular, doxycycline is used for the treatment of chronic prostatitis, sinusitis, syphilis, pelvic inflammatory disease, oral ulcers, oral herpes simplex infections and for acne vulgaris. It is also used for the treatment and prophylaxis of malaria.

EXPERT REPORT

The CV of the medical expert indicates that she is a physician with suitable qualifications and experience to assume the role of clinical expert. The CV of the pharmaceutical expert indicates that he is a pharmacist with nearly twenty years' experience in quality control, production and pharmaceutical development. The CV indicates that he is suitably qualified for the role of pharmaceutical expert.

MARKETING AUTHORISATION APPLICATION (MAA)

The MAA form submitted with this application is satisfactory.

ACTIVE INGREDIENT SOURCE

The source of active ingredient is also listed on the licence of the cross-reference product. A copy of the EDQM Certificate of Suitability (R2-CEP 1992-018-Rev 00) for the supplier is provided, which is current and satisfactory.

A drug substance specification for doxycycline hyclate has been provided by the applicant that complies with the BP monograph. This is acceptable.

MANUFACTURER

The two sites of manufacture stated in the MAA form are identical to those on the licence of the cross-reference product. Appropriate manufacturing authorisations are provided.

A statement of willingness to manufacture the product is provided from the manufacturer.

A flow chart detailing the sites involved in the manufacturing process has been supplied. Other sites have been specified as storage, distribution and batch release sites. Appropriate manufacturing authorisations are provided. Batch release is carried out by Klocke Verpackungs Service GmbH.

MANUFACTURING PROCESS

The qualitative and quantitative composition of the product is the same as that of the cross-reference product.

The manufacturing process for the maximum batch size has been outlined and is identical to that of the cross-reference product.

PRODUCT SPECIFICATIONS

The finished product specifications at release and shelf life are provided. All tests and limits are satisfactory.

STORAGE DETAILS

The shelf lives and storage conditions for the applicant's product are identical to those of the cross-reference product and are 36 months (3 years) with no special precautions for storage. These are in agreement with the SPCs.

PACKAGING

The packaging is identical to that described for the cross-reference product (blister).

PACK SIZES

The proposed blister pack sizes are 8, 10 and 50 capsules. These are the same as the cross-reference product.

TSE COMPLIANCE

Compliance with TSE requirements for gelatin for the capsule shells has been demonstrated by the provision of Ph.Eur. Certificates of Suitability, copies of which have been provided. The certificates from the three specified suppliers of capsule shells are up-to-date and satisfactory.

OTHER INFORMATION

The qualified person nominated to be responsible for pharmacovigilance matters is suitably qualified.

SUMMARY OF PRODUCT CHARACTERISTICS
The SPC is based on that of the cross-reference product. This is in line with current guidelines.

LEAFLET AND LABELLING
Leaflet mock-ups have been provided, which are consistent with the SPC and are satisfactory in terms of content and readability.

Full colour, actual size mock-ups of the carton and blister are provided.

CONCLUSION
A product licence may be granted.

NON-CLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none is required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none is required for an application of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

NON-CLINICAL

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

EFFICACY AND SAFETY

The efficacy of doxycycline has been well documented in the past. No new or unexpected safety
concerns arise from this application.
The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The risk benefit ratio is considered to be positive.

DOXYCYCLINE 100 MG CAPSULES

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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application on 20 August 2003
2	Following assessment of the application the MHRA requested further information relating to the quality dossier on 3 March 2004
3	The applicant responded to the MHRA's requests, providing further information on 6 August 2004
4	Following assessment of the response the MHRA requested further information relating to the quality dossier on 15 December 2004
5	The applicant responded to the MHRA's requests, providing further information on 16 February 2006
6	Following assessment of the response the MHRA requested further information relating to the quality dossier on 19 June 2006
7	The applicant responded to the MHRA's requests, providing further information on 20 September 2006
8	Following assessment of the response the MHRA requested further information relating to the quality dossier on 20 September 2006
9	The applicant responded to the MHRA's requests, providing further information on 19 October 2006
10	The application was determined on 24 October 2006

Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The SmPC and PIL are consistent with the details registered for the cross-reference products.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The following text is the approved label text for this medicine, no label mock-ups have been provided. In accordance with medicines legislation, the product shall not be marketed in the UK until approval of the label mock-ups has been obtained:

LABELLING

Carton Labelling Text

1. NAME OF THE MEDICINAL PRODUCT

Doxycycline 100 mg capsules

2. STATEMENT OF ACTIVE SUBSTANCES

Each capsule contains 115.40 mg doxycycline hyclate, equivalent to 100 mg doxycycline base.

3. LIST OF EXCIPIENTS

Also contains sucrose

4. PHARMACEUTICAL FORM AND CONTENTS

Capsules: 8 Capsules
Capsules: 50 Capsules

5. METHOD AND ROUTES OF ADMINISTRATION

Swallow whole with a glass of water, do not bite crush or chew

Read the information leaflet carefully before use

6. SPECIAL WARNINGS THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep medicines out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S) , IF NECCESARY

-

8. EXPIRY DATE

Exp: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

-

10. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited,
Polhampton Lane, Overton Hampshire,
RG25 3ED, UK

11. MARKETING AUTHORISATION NUMBER

PL 20416/0460

12. MANUFACTURERS BATCH NUMBER

BN: XXXX

13. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

POM

14. OTHER

Swallow whole with a glass of water, do not bite crush or chew

15. INSTRUCTIONS FOR USE

Take as directed by your doctor

Label Text - Blisters

1. NAME OF THE MEDICINAL PRODUCT

Doxycycline 100 mg capsules

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited

3. EXPIRY DATE

Exp: MM/YYYY

4. BATCH NUMBER

BN: XXXX

Annex 1

Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

Scope	**Procedure number**	**Product information affected**	**Date of start of the procedure**	**Date of end of procedure**	**Approval/ non approval**	**Assessment report attached Y/N (version)**
To update SmPC sections 2.0, 4.1, 4.2, 4.3, 4.4, 4.6, 4.8, 5.1, 5.2 and 6.5 with consequential changes to the PIL in order to include paediatric information following publication of the Public Assessment Report for paediatric studies from procedure UK/W/0090/pdWS/001. Editorial and QRD template changes are also made.	PL 20416/0460-0008	SmPC and PIL	N/A	N/A	Approved on 25/06/2018	Y-see Annex 1

ANNEX 1

Our Reference:	PL 20416/0460-0008
Product:	Doxycycline 100mg Capsules
Marketing Authorisation Holder:	Crescent Pharma Limited
Active Ingredient(s):	Doxycycline hyclate
Type of Procedure:	National
Submission Type:	Variation
Submission Category:	Type IB
Submission Complexity:	Standard
EU Procedure Number (if applicable):	Not applicable

Reason:
To update SmPC sections 2.0, 4.1, 4.2, 4.3, 4.4, 4.6, 4.8, 5.1, 5.2 and 6.5 with consequential changes to the PIL in order to include paediatric information following publication of the Public Assessment Report for paediatric studies from procedure UK/W/0090/pdWS/001. Editorial and QRD template changes are also made.

Supporting Evidence
Revised SmPC fragments and PIL.

Evaluation
The proposed changes to the SmPC and PIL are acceptable. The updated SmPC fragments and PIL have been incorporated into the Marketing Authorisation.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

Conclusion
The proposed changes to the SmPC and PIL are acceptable.

Decision - Approved on 25 June 2018.