TABLE OF CONTENTS

Lay Summary ............................................................ Page 2
Scientific discussion .................................................... Page 3
Steps taken for assessment .......................................... Page 8
Steps taken after authorisation – summary .................. Page 9
Summary of Product Characteristics .........................
Product Information Leaflet ......................................
Labelling .................................................................
CETIRIZINE DIHYDROCHLORIDE 10MG FILM-COATED TABLETS
PL 40378/0140-1

LAY SUMMARY

On 5 November 2012, the MHRA granted APTIL Pharma Limited Marketing Authorisations (licences) for the medicinal products Cetirizine Dihydrochloride 10mg film-coated tablets (PL 40378/0140-1). These are pharmacy (legal status P) and general sales licence (legal status GSL) medicines containing the active ingredient cetirizine dihydrochloride. Cetirizine is an antiallergic medication. In adults and children aged 6 years and above, cetirizine is indicated for the relief of:

- hayfever (allergic rhinitis) and year round allergies, such as dust or pet allergies (perennial allergic rhinitis)
- chronic nettle rash (chronic idiopathic urticaria)

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Cetirizine Dihydrochloride 10mg film-coated tablets outweigh the risks, hence Marketing Authorisations have been granted.
CETIRIZINE DIHYDROCHLORIDE 10MG FILM-COATED TABLETS
PL 40378/0140-1

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>Pharmaceutical assessment</td>
<td>5</td>
</tr>
<tr>
<td>Preclinical assessment</td>
<td>7</td>
</tr>
<tr>
<td>Clinical assessment (including statistical assessment)</td>
<td>7</td>
</tr>
<tr>
<td>Overall conclusions and risk benefit assessment</td>
<td>7</td>
</tr>
</tbody>
</table>
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted Marketing Authorisations for the medicinal products Cetirizine Dihydrochloride 10mg film-coated tablets (PL 40378/0140-1) on 5 November 2012 to APTIL Pharma Limited.

These are applications for Cetirizine Dihydrochloride 10mg film-coated tablets (PL 40378/0140-1), submitted as abridged simple applications according to Article 10c of Directive 2001/83/EC, cross-referring to Cetirizine Dihydrochloride 10mg Film-Coated Tablets (PL 33410/0043 & 0062), which was originally granted licences to APSLA Limited in June 2011.

Cetirizine, a metabolite of hydroxyzine, is a non-sedative second-generation histamine H1-antagonist, widely used in human medicine to treat seasonal/perennial allergic rhinitis and chronic idiopathic urticaria. Cetirizine also displays high and selective affinity for cloned human H1-histamine receptors and it has very little or no anti-cholinergic activity.

These are pharmacy (legal status P) and general sales licence (legal status GSL) medicines, indicated for the symptomatic treatment of perennial rhinitis, seasonal allergic rhinitis and chronic idiopathic urticaria.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 40378/0140-1
PROPRIETARY NAME: Cetirizine Dihydrochloride 10mg film-coated tablets
ACTIVE(S): Cetirizine dihydrochloride
COMPANY NAME: APTIL Pharma Limited
LEGAL STATUS: P

1. INTRODUCTION
These are simple, piggyback applications for Cetirizine Dihydrochloride 10mg film-coated tablets submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is APTIL Pharma Limited, 9th Floor, CP House, 97–107 Uxbridge Road, Ealing, London W5 5TL.

The applications cross-refer to Cetirizine Dihydrochloride 10mg Film-Coated Tablets (PL 33410/0043 & 0062), which was originally granted a licence to APSLA Limited in June 2011.

The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A suitable justification has been provided for non-submission of a Risk Management Plan (RMP). As these are abridged simple applications containing an active ingredient that has been used for many years and has a well-established safety profile, an RMP is not considered necessary.

A suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As these products are intended for substitution with products that are already currently marketed, there is considered to be no increase in environmental burden and an RMP is not considered necessary.

The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 NAME(S)
The proposed name of the products is Cetirizine Dihydrochloride 10mg film-coated tablets. The products have been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each film-coated tablet contains 10mg cetirizine dihydrochloride. They are to be packed in aluminium/polyvinylchloride blister packs in pack sizes of:

PL 40378/0140: 7, 14, 21, 28, 30 or 60 film-coated tablets.
PL 40378/0141: 4, 5, 7 or 14 film-coated tablets
The proposed shelf-life (3 years) and storage conditions (Keep the blister in the outer carton in order to protect from light) are consistent with the details registered for the cross-reference products.

2.3 Legal status
On approval, the products will be available as pharmacy (legal status P) and general sales licence (legal status GSL) medicines.

2.4 Marketing authorisation holder/Contact Persons/Company
APTIL Pharma Limited, 9th Floor, CP House, 97–107 Uxbridge Road, Ealing, London W5 5TL.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference products.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference products.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
No materials of animal or human origin are included in this product. This is consistent with the cross-reference products.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the products is identical to the cross-reference products.
5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPCs are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL)/CARTON
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference products.

Carton and blister
The proposed artwork is comparable to the artwork registered for the cross-reference products and complies with statutory requirements. In-line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with these applications are acceptable. From a quality perspective, Marketing Authorisations should be granted.

NON-CLINICAL ASSESSMENT
No new non-clinical data have been supplied with these applications and none are required for applications of this type.

CLINICAL ASSESSMENT
No new clinical data have been supplied with these applications and none are required for applications of this type.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Cetirizine Dihydrochloride 10mg film-coated tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

CLINICAL PHARMACOLOGY/EFFICACY
No new clinical pharmacology/efficacy data have been submitted with these applications and none are required for applications of this type.

SAFETY
No new safety data have been submitted with these applications and none are required for applications of this type.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with cetirizine is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
CETIRIZINE DIHYDROCHLORIDE 10MG FILM-COATED TABLETS

STEPS TAKEN FOR ASSESSMENT

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 10 July 2012</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant, the MHRA considered the application valid on 16 July 2012</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application, the MHRA requested further information relating to the dossiers on 7 August 2012</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 20 August 2012</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 5 November 2012</td>
</tr>
</tbody>
</table>
CETIRIZINE DIHYDROCHLORIDE 10MG FILM-COATED TABLETS

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Summary of Product Characteristics and Patient Information Leaflet
The current approved UK versions of the Summary of Product Characteristics (SmPCs) and Patient Information Leaflet (PILs) for these products is available on the MHRA website.