Oxybutynin hydrochloride 2.5 mg tablets
Oxybutynin hydrochloride 3 mg tablets
Oxybutynin hydrochloride 5 mg tablets

PL 20117/0200-2

UKPAR

TABLE OF CONTENTS

Lay Summary Page 2
Scientific discussion Page 3
Steps taken for assessment Page 14
Steps taken after authorisation – summary
Summary of Product Characteristics Page 15
Patient Information Leaflet Page 16
Labelling Page 17
Oxybutynin hydrochloride 2.5 mg tablets
Oxybutynin hydrochloride 3 mg tablets
Oxybutynin hydrochloride 5 mg tablets

PL 20117/0200-2

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Morningside Healthcare Limited Marketing Authorisations for the medicinal products Oxybutynin hydrochloride 2.5 mg, 3 mg and 5 mg tablets (PL 20117/0200-2) on 16 July 2013. These medicines are only available on prescription from your doctor. Oxybutynin hydrochloride 2.5 mg, 3 mg and 5 mg tablets may be prescribed by the doctor for the treatment of the involuntary loss of urine as a result of an unstable or over-active bladder; in other words, when it is not possible to keep the urge to urinate and the frequent need to urinate normally under control.

The active ingredine is oxybutynin hydrochloride. Oxybutynin hydrochloride tablets belong to the group of spasm-relieving agents (a so-called spasmolytic). Oxybutynin hydrochloride tablets act by reducing the muscle spasms of the bladder. It is these spasms that cause the feeling of having to urinate frequently, which in turn can lead to involuntary loss of urine. Oxybutynin hydrochloride relaxes the bladder muscle, so that the bladder can hold more urine and the frequent urge to urinate is reduced.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Oxybutynin hydrochloride 2.5 mg, 3 mg and 5 mg tablets outweigh the risks and Marketing Authorisations were granted.
Table of Contents

Introduction Page 4
Pharmaceutical assessment Page 5
Non-clinical assessment Page 7
Clinical assessment Page 8
Overall conclusions and risk assessment Page 13
INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Morningside Healthcare Limited Marketing Authorisations for the medicinal products Oxybutynin hydrochloride 2.5 mg, 3 mg and 5 mg tablets (PL 20117/0200-2). These products are prescription-only medicines (POM).

Oxybutynin hydrochloride 2.5 mg, 3 mg and 5 mg tablets are indicated for urinary incontinence, urgency and frequency in unstable bladder, whether due to neurogenic bladder disorders (detrusor hyperreflexia) in conditions such as multiple sclerosis and spina bifida, or to idiopathic detrusor instability (motor urge incontinence).

Oxybutynin hydrochloride is indicated in children over 5 years of age for:
Urinary incontinence, urgency and frequency in unstable bladder conditions due to idiopathic overactive bladder or neurogenic bladder disorders (detrusor overactivity).

These applications were submitted under Article 10(1) of Directive 2001/83/EC, as amended. The applications for Oxybutynin hydrochloride 2.5 mg and 5 mg tablets cross-refer to Ditropan 2.5mg tablet (PL 04425/0289, Sanofi Aventis) and Ditropan 5mg tablet (PL 04425/0290; Sanofi-Aventis, UK), which were first authorised in the UK on 01 May 1997. The application for Oxybutynin hydrochloride 3 mg tablets cross-refer to Cystrin 3mg tablets (PL 11723/0343; Sanofi-Aventis, UK) and PL 17780/0532; Winthrop Pharmaceuticals UK Limited, UK),which was first authorised in the UK on 25 March 2009. The application for Oxybutynin hydrochloride 3 mg tablets also cross-refer to Cystrin 3mg tablets (PL 11723/0343; Sanofi-Aventis, UK) which previously was authorised to Sanofi-Aventis (PL 11723/0343).

The active ingredient, oxybutynin hydrochloride, is a tertiary amine anticholinergic agent which exerts antimuscarinic as well as direct antispasmodic action on smooth muscle. In addition to its smooth muscle relaxing effects, oxybutynin hydrochloride exerts an analgesic and a local anaesthetic effect. The mechanisms of action are believed to be through:
• a direct antispasmodic effect on bladder smooth muscle;
• competitive antagonism of acetylcholine at post-ganglionic muscarinic receptors.

Two bioequivalence studies were submitted to support these applications, comparing the applicant’s test product Oxybutynin hydrochloride 5 mg tablet with the reference product Ditropan 5mg tablets (Sanofi-Aventis, UK). The bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP).

With the exception of the bioequivalence studies, no new non-clinical or clinical data were submitted, which is acceptable given that the applications were based on the products being generic medicinal products of an originator products that have been in clinical use for over 10 years.

No new or unexpected safety concerns arose during review of information provided by the Marketing Authorisation Holder and it was, therefore, judged that the benefits of taking Oxybutynin hydrochloride 2.5 mg, 3 mg and 5 mg tablets outweigh the risks and Marketing Authorisations were granted.
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE

INN: Oxybutynin hydrochloride

Chemical name: 4-(diethylamino)-2-butynyl-α-phenyl-cyclohexaneglycolate hydrochloride

Structure:

Molecular formula: C_{22}H_{31}NO_3.HCl
Molecular weight: 393.95

Appearance: White to off white powder.

Solubility: Freely soluble in water and ethanol; very soluble in methanol and chloroform; soluble in acetone; slightly soluble in ether and in hexane.

Oxybutynin hydrochloride is the subject of a European Pharmacopoeia monograph.

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

DRUG PRODUCT

Other Ingredients

Other ingredients consist of the pharmaceutical excipients crospovidone, microcrystalline cellulose, lactose monohydrate and magnesium stearate. Appropriate justification for the inclusion of each excipient has been provided.

All excipients comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients, showing compliance with the proposed specifications.

With the exception of lactose monohydrate, none of the excipients contain materials of animal or human origin. The supplier of lactose monohydrate has confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the supplier has confirmed that no ruminant material other than calf rennet is used during the production of lactose monohydrate.

No genetically modified organisms (GMO) have been used in the preparation of these excipients.

Pharmaceutical Development

The objective of the development programme was to formulate safe, efficacious, stable products comparable in performance to the oxybutynin tablet preparations (e.g. Ditropan and Cystrin) manufactured by Sanofi- Aventis and marketed in the EU.

Suitable pharmaceutical development data have been provided for these applications.

Comparative in-vitro dissolution profiles have been provided for these products and the reference products.
Manufacturing Process
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing processes. The manufacturing processes have been validated with full-scale production batches and have shown satisfactory results.

Control of Finished Product
The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Container Closure System
The tablets are packaged in aluminium/polyvinyl chloride/polyvinylidene chloride blisters packed in cartons, with a Patient Information Leaflet, in pack sizes of 7, 28, 56 and 84 tablets.

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 European regulations concerning materials in contact with food.

Stability
Finished product stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 3 years, with the storage conditions ‘Do not store above 25°C. Store in the original package. Keep out of the sight and reach of children.’

Bioequivalence
Satisfactory Certificates of Analysis have been provided for the test and reference batches used in the bioequivalence study.

Summaries of Product Characteristics (SmPCs), Patient Information Leaflets (PILs) and Labels
The SmPCs, PILs and labels are satisfactory from a pharmaceutical perspective.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA (Marketing Authorisation Application) Form
The MAA forms are satisfactory from a pharmaceutical perspective.

Expert Report (Quality Overall Summary)
The quality overall summary is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

PHARMACODYNAMICS, PHARMACOKINETICS AND TOXICOLOGY
As the pharmacodynamic, pharmacokinetic and toxicological properties of oxybutynin hydrochloride are well-known, no further non-clinical studies are required and none have been provided.

NON-CLINICAL EXPERT REPORT (NON-CLINICAL OVERVIEW)
The applicant’s non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

ENVIRONMENTAL RISK ASSESSMENT
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As these products are intended for generic substitution with products that are already marketed, no increase in environmental burden is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

CONCLUSION
The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
The clinical pharmacology of oxybutynin hydrochloride is well-known. With the exception of data from the bioequivalence studies detailed below, no new pharmacodynamic or pharmacokinetic data are provided or are required for these applications.

Pharmacokinetics
In support of the applications, the applicant submitted the following bioequivalence studies:

Study 1
A randomised, open label, single dose, 2-way, crossover single-dose study to compare the pharmacokinetics of the test product Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands) versus the reference product Ditropan 5 mg tablets (Sanofi-Aventis, UK) in healthy male and female subjects under fasting conditions.

The subjects were administered 10 mg (two tablets) of either the test or the reference product with approximately 240 ml of water, after at least a 10-hour overnight fast. Blood samples were collected before and up to and including 24 hours after each administration. The washout period between the treatment phases was 5 days. The pharmacokinetic results for R-oxybutynin, S-oxybutynin, R-N-Desethyloxybutynin and S-N-Desethyloxybutynin are presented below:

R-Oxybutynin

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Summary of pharmacokinetic results for each treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parameters</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (ng/mL)</td>
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<tr>
<td>T&lt;sub&gt;max&lt;/sub&gt; (h)</td>
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<tr>
<td>AUC&lt;sub&gt;last&lt;/sub&gt; (ng h/mL)</td>
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<tr>
<td>AUC&lt;sub&gt;tot&lt;/sub&gt; (ng h/mL)</td>
<td>12.56</td>
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<tr>
<td>%AUC&lt;sub&gt;extra&lt;/sub&gt;</td>
<td>8.95</td>
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</table>

C<sub>max</sub> maximum plasma concentration observed following administration of dose
AUC<sub>last</sub> area under the plasma concentration-time curve from time zero to last observed concentration at time t
AUC<sub>tot</sub> AUC<sub>last</sub> + AUC<sub>extra</sub> (corresponds to AUC<sub>tot</sub> in pharmacokinetic output)
Reference product (Ditropan 5 mg tablets (Sanofi-Aventis, UK)
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands)

S-Oxybutynin

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Summary of pharmacokinetic results for each treatment</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Parameters</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (ng/mL)</td>
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<td>T&lt;sub&gt;max&lt;/sub&gt; (h)</td>
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<tr>
<td>AUC&lt;sub&gt;last&lt;/sub&gt; (ng h/mL)</td>
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<td>AUC&lt;sub&gt;tot&lt;/sub&gt; (ng h/mL)</td>
<td>2.05</td>
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</table>

C<sub>max</sub> maximum plasma concentration observed following administration of dose
AUC<sub>last</sub> area under the plasma concentration-time curve from time zero to last observed concentration at time t
AUC<sub>tot</sub> AUC<sub>last</sub> + AUC<sub>extra</sub> (corresponds to AUC<sub>tot</sub> in pharmacokinetic output)
Reference product (Ditropan 5 mg tablets (Sanofi-Aventis, UK)
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands)
R-N-Oxybutynin

Summary of pharmacokinetic results for each treatment

<table>
<thead>
<tr>
<th>Parameters</th>
<th>TEST</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN</td>
<td>C.V. (%)</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (ng/mL)</td>
<td>35.40</td>
<td>33.19</td>
</tr>
<tr>
<td>T&lt;sub&gt;max&lt;/sub&gt; (h)</td>
<td>1.05</td>
<td>68.44</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;last&lt;/sub&gt; (ng·h/mL)</td>
<td>234.95</td>
<td>60.00</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;tot&lt;/sub&gt; (ng·h/mL)</td>
<td>241.97</td>
<td>69.81</td>
</tr>
</tbody>
</table>

C<sub>max</sub> maximum plasma concentration observed following administration of dose
AUC<sub>last</sub> area under the plasma concentration-time curve from time zero to last observed concentration at time t
AUC<sub>tot</sub> AUC<sub>last</sub> + AUC<sub>extra</sub> (corresponds to AUC<sub>tot</sub> in pharmacokinetic output).
Reference product (Ditropan 5 mg tablets (Sanofi-Aventis, UK))
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands))

S-N-Oxybutynin

Summary of pharmacokinetic results for each treatment

<table>
<thead>
<tr>
<th>Parameters</th>
<th>TEST</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN</td>
<td>C.V. (%)</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (ng/mL)</td>
<td>30.45</td>
<td>35.07</td>
</tr>
<tr>
<td>T&lt;sub&gt;max&lt;/sub&gt; (h)</td>
<td>1.19</td>
<td>69.58</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;last&lt;/sub&gt; (ng·h/mL)</td>
<td>134.75</td>
<td>53.27</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;tot&lt;/sub&gt; (ng·h/mL)</td>
<td>140.30</td>
<td>53.19</td>
</tr>
</tbody>
</table>

C<sub>max</sub> maximum plasma concentration observed following administration of dose
AUC<sub>last</sub> area under the plasma concentration-time curve from time zero to last observed concentration at time t
AUC<sub>tot</sub> AUC<sub>last</sub> + AUC<sub>extra</sub> (corresponds to AUC<sub>tot</sub> in pharmacokinetic output).
Reference product (Ditropan 5 mg tablets (Sanofi-Aventis, UK))
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands))

Comparision of standards for Bioequivalence Test/Reference

Comparision of standards for Bioequivalence Test/Reference R-Oxybutynin

PK Variables | Geometric mean ratio or point estimator | 90% confidence limits | CV% Within subject
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (ratio test / ref)</td>
<td>1.1329</td>
<td>1.0141 - 1.2656</td>
<td>40.98</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;last&lt;/sub&gt; (ratio test / ref)</td>
<td>1.0636</td>
<td>0.9873 - 1.1458</td>
<td>27.54</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;tot&lt;/sub&gt; (ratio test / ref)</td>
<td>1.0620</td>
<td>0.9913 - 1.1377</td>
<td>25.50</td>
</tr>
</tbody>
</table>

C<sub>max</sub> maximum plasma concentration observed following administration of dose
AUC<sub>tot</sub> area under the plasma concentration-time curve from time zero to t hours
AUC<sub>last</sub> area under the plasma concentration-time curve from time zero to last observed concentration at time t
Reference product (Ditropan 5 mg tablets (Sanofi-Aventis, UK))
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands))
Comparision of standards for Bioequivalence Test/Reference S-Oxybutynin

<table>
<thead>
<tr>
<th>PK Variables</th>
<th>Geometric mean ratio or point estimator</th>
<th>90% confidence limits</th>
<th>CV% Within subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{max}$ (ratio test / ref)</td>
<td>1.1172</td>
<td>0.99501 - 1.2543</td>
<td>42.86</td>
</tr>
<tr>
<td>$AUC_{tot}$ (ratio test / ref)</td>
<td>1.0730</td>
<td>0.9997 - 1.1517</td>
<td>26.19</td>
</tr>
<tr>
<td>$AUC_{last}$ (ratio test / ref)</td>
<td>1.0788</td>
<td>1.0049 - 1.1582</td>
<td>26.26</td>
</tr>
</tbody>
</table>

*units are ng/mL for $C_{max}$ and ng.h/mL for $AUC_{tot}$ and $AUC_{last}$

$C_{max}$ maximum plasma concentration observed following administration of dose
$AUC_{tot}$ area under the plasma concentration-time curve from time zero to t hours
$AUC_{last}$ area under the plasma concentration-time curve from time zero to last observed concentration at time t
Reference product (Ditropan 5 mg tablets (Sanofi-Aventis, UK))
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands))
CV coefficient of variation

Conclusion
The Note for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1) defines the confidence limits as 80.00 to 125.00 % for AUC and $C_{max}$ values. The 90% confidence intervals for AUC for R-Oxybutynin and S-Oxybutynin and $C_{max}$ for S-Oxybutynin lie within the accepted range of 80.00% -125.00%. However, as the 90% confidence intervals for $C_{max}$ for R-Oxybutynin do not lie within the acceptable limits of 80.00% to 125.00%, the applicant was requested to submit further data. In response to the assessor’s request the MAH submitted an additional bioequivalence study based on a racemic assay of oxybutynin.

Study 2
A randomised, open label, two-treatment, two-sequence, two-period, crossover single-dose study to compare the pharmacokinetics of the test product Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands) versus the reference product Ditropan 5 mg tablets (Sanofi-Aventis, UK) in healthy male subjects under fasting conditions.

The subjects were administered one tablet of either the test or the reference product with approximately 240 ml of water, after at least a 10-hour overnight fast. Blood samples were collected before and up to and including 24 hours after each administration. The washout period between the treatment phases was 8 days. The pharmacokinetic results for oxybutynin and its active metabolite, N-desethyloxybutynin are presented below:

For Oxybutynin:

Summary of pharmacokinetic results (arithmetic means±standard deviation) for each treatment

<table>
<thead>
<tr>
<th>Arithmetic mean±SD</th>
<th>Reference product (R)</th>
<th>Test product (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{max}$ (ng/mL)</td>
<td>14.771±10.9707</td>
<td>14.642±10.0215</td>
</tr>
<tr>
<td>$AUC_{tot}$ (hr*ng/mL)</td>
<td>30.457±23.6629</td>
<td>29.439±20.6845</td>
</tr>
<tr>
<td>$AUC_{last}$ (hr*ng/mL)</td>
<td>33.527±27.7611</td>
<td>32.192±23.4976</td>
</tr>
</tbody>
</table>

$C_{max}$ maximum plasma concentration
$AUC_{tot}$ area under the plasma concentration-time curve from time zero to t hours
$AUC_{last}$ area under the plasma concentration-time curve from time zero to infinity
SD standard deviation
Reference product (Ditropan 5 mg tablets (Sanofi Winthrop Industries, France))
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands))
For N-desethyloxybutynin:

Summary of pharmacokinetic results (arithmetic means±standard deviation) for each treatment

<table>
<thead>
<tr>
<th>Arithmetic mean±SD</th>
<th>Reference product (R)</th>
<th>Test product (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(C_{\text{max}}) (ng/mL)</td>
<td>93.872±28.5432</td>
<td>91.586±26.4316</td>
</tr>
<tr>
<td>(AUC_{0-t}) (hr*ng/mL)</td>
<td>393.880±201.0112</td>
<td>385.067±192.4229</td>
</tr>
<tr>
<td>(AUC_{0-\infty}) (hr*ng/mL)</td>
<td>407.035±219.9581</td>
<td>395.635±205.538</td>
</tr>
</tbody>
</table>

For N-desethyloxybutynin:

Summary of pharmacokinetic results (arithmetic means±standard deviation) for each treatment

<table>
<thead>
<tr>
<th>Arithmetic mean±SD</th>
<th>Reference product (R)</th>
<th>Test product (T)</th>
</tr>
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<tbody>
<tr>
<td>(C_{\text{max}}) (ng/mL)</td>
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<tr>
<td>(AUC_{0-\infty}) (hr*ng/mL)</td>
<td>407.035±219.9581</td>
<td>395.635±205.538</td>
</tr>
</tbody>
</table>

C\(_{\text{max}}\) maximum plasma concentration
A\(_{\text{UC}}\) area under the plasma concentration-time curve from time zero to t hours
A\(_{\text{UC}}\) area under the plasma concentration-time curve from time zero to infinity
SD standard deviation
Reference product (Ditropan 5 mg tablets (Sanofi Winthrop Industries, France)
Test product (Oxybutynin hydrochloride 5 mg tablet (FAL Duiven BV, The Netherlands)

Pharmacokinetic parameters (geometric least square means ratios and confidence intervals [CI]) for oxybutynin

<table>
<thead>
<tr>
<th>Geometric Least Square Means Ratio (T/R) (%)</th>
<th>Intra-subject CV (%)</th>
<th>90% CI</th>
<th>Power (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>98.79</td>
<td>34.75</td>
<td>89.94-108.51</td>
<td>98.77</td>
</tr>
<tr>
<td>98.14</td>
<td>25.57</td>
<td>91.51-105.25</td>
<td>99.98</td>
</tr>
<tr>
<td>97.87</td>
<td>25.47</td>
<td>91.28-104.93</td>
<td>99.98</td>
</tr>
</tbody>
</table>

C\(_{\text{max}}\) maximum plasma concentration
A\(_{\text{UC}}\) area under the plasma concentration-time curve from time zero to t hours
A\(_{\text{UC}}\) area under the plasma concentration-time curve from time zero to infinity
SD standard deviation
CV coefficient of variation

Overall bioequivalence conclusion

The Note for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1) defines the confidence limits as 80.00 to 125.00 % for AUC and \(C_{\text{max}}\) values. The 90% confidence intervals for the ratio of the AUC and \(C_{\text{max}}\) for oxybutynin lie within the acceptance criteria. Thus, the data generated from Study 2 support the claim that the applicant’s test product is bioequivalent to the reference product Ditropan 5 mg tablets (Sanofi-Aventis, UK) under fasting conditions.

A biowaiver has been granted to the 2.5 mg and 3 mg strength tablets based on the study conducted, in line with the current bioequivalence guideline.

Efficacy

The efficacy of oxybutynin hydrochloride is well-known. No new efficacy data have been submitted and none are required for applications of this type.

Safety

With the exception of the safety data generated during the bioequivalence studies, no new safety data were submitted and none are required for applications of this type. No new or unexpected safety issues arose during the bioequivalence studies.
PHARMACOVIGILANCE SYSTEM AND RISK MANAGEMENT PLAN
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.

Suitable justification has been provided for not submitting a Risk Management Plan for this product.

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs), PATIENT INFORMATION LEAFLETS (PILs) AND LABELLING
The SmPCs, PILs and labelling are satisfactory from a clinical perspective. The SmPCs are consistent with those for the reference products. The PILs are consistent with the details in the SmPCs and in line with the current guidance. The labelling is in line with current guidance.

CLINICAL EXPERT REPORT (CLINICAL OVERVIEW)
The clinical overview is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

CONCLUSION
The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT
QUALITY
The important quality characteristics of Oxybutynin hydrochloride 2.5mg, 3 mg and 5 mg 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. As the pharmacokinetics, pharmacodynamics and toxicology of oxybutynin hydrochloride are well-known, no additional data were required.

EFFICACY
With the exception of the bioequivalence studies, no new data were submitted and none are required for applications of this type.

Bioequivalence has been demonstrated between the applicant’s product and the reference product Ditropan 5 mg tablets (Sanofi-Aventis, UK) under fasting conditions.

A biowaiver has been granted to the 2.5 mg and 3 mg strength tablets based on the data submitted, in line with the current bioequivalence guideline.

SAFETY
With the exception of the safety data from the bioequivalence studies, no new data were submitted and none are required for this type of application. As the safety profile of oxybutynin hydrochloride is well-known, no additional data were required. No new or unexpected safety concerns arose from the safety data from the bioequivalence study.

PRODUCT LITERATURE
The SmPCs, PILs and labelling are acceptable. The SmPCs are consistent with those for the reference products. The PILs are consistent with the details in the SmPCs and in line with the current guidance. The labelling is in line with current guidance.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with oxybutynin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Oxybutynin hydrochloride 2.5 mg tablets
Oxybutynin hydrochloride 3 mg tablets
Oxybutynin hydrochloride 5 mg tablets

PL 20117/0200-2

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Marketing Authorisation applications on 17 January 2011.
2. Following standard checks and communication with the applicant the MHRA considered the applications valid on 07 February 2011.
4. The applicant responded to the MHRA’s requests, providing further information on the clinical dossier on 30 November 2012 and on the quality dossier on 15 August 2012, 20 September 2012, 02 April 2013 and 30 May 2013.
5. The applications were granted on 16 July 2013.
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
Each tablet contains 2.5mg of oxybutynin hydrochloride.

Contains lactose. See leaflet for further information.

For oral administration.

Dosage to be taken as directed by your doctor.

Keep out of the sight and reach of children.

Do not store above 25°C.
Each tablet contains 5 mg of oxybutynin hydrochloride.
Contains lactose. See leaflet for further information.
For oral administration.
Dosage to be taken as directed by your doctor.

Keep out of the sight and reach of children.
Do not store above 25°C.