Public Assessment Report

Decentralised Procedure

Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets

Procedure No: UK/H/4082/001-004/DC

UK Licence No: PL 03525/0009-0012

EGIS Pharmaceuticals PLC
Lay Summary
Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets (olanzapine)

This is a summary of the Public Assessment Report (PAR) for Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets (PL 03525/0009-0012; UK/H/4082/001-004/DC). It explains how Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets.

For practical information about using Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets and what are they used for?
Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are ‘generic medicines’. This means that they are similar to ‘reference medicines’, already authorised in the European Union (EU) called Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets.

Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are used to treat the following conditions:
- Schizophrenia; a disease with symptoms such as hearing, seeing or sensing things which are not there, mistaken beliefs, unusual suspiciousness, and becoming withdrawn. People with this disease may also feel depressed, anxious or tense.
- Moderate to severe manic episodes; a condition with symptoms of excitement or euphoria. Olanzapine has been shown to prevent recurrence of these symptoms in patients with bipolar disorder whose manic episode has responded to olanzapine treatment.

How do Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets work?
Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets contain the active substance olanzapine, which belongs to a group of medicines called antipsychotics; the precise way in which olanzapine works is not fully understood.

How are Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets used?
Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets can either be placed on the tongue, where they will dissolve directly into the mouth for easy swallowing, or they can be placed in a full glass or cup of water, orange juice, apple juice, milk or coffee. When dissolving the orodispersible tablet in a glass or cup, the drink should be stirred and swallowed straight away. Olanzapine orodispersible tablets can break easily and so should be handled carefully, with dry hands.

Please read Section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration and the duration of treatment.

The daily dose of Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets is between 5 and 20 mg but your doctor will decide how many orodispersible tablets to take and for how long. Olanzapine is not intended for patients who are under 18 years of age.
This medicine can only be obtained with a prescription.

**How have Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets been studied?**
Because Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are generic medicines, studies in patients have been limited to tests to determine that Olanzapine 5 mg orodispersible tablets are bioequivalent to the reference medicine, Zyprexa Velotab 5 mg orodispersible tablets. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

It was deduced from these tests that Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are comparable to equivalent strengths of the reference medicines Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets.

**What are the possible side effects of Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets?**
Because Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are generic medicines, their benefits and possible side effects are taken as being the same as those of the reference medicines, Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets.

For further information, please see the package leaflet.

**Why are Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets approved?**
It was concluded that, in accordance with EU requirements, Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets have been shown to have comparable quality and be bioequivalent to Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets. Therefore, the view was that, as for Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets, the benefits outweigh the identified risks and Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets can be approved for use.

**What measures are being taken to ensure the safe and effective use of Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets?**
Known side effects are continuously monitored. Furthermore new safety signals reported by patients and healthcare professionals will be monitored and reviewed continuously as well.

**Other information about Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets**
Bulgaria, the Czech Republic, Hungary, Latvia, Lithuania, Poland, Romania and the Slovak Republic and the UK agreed to grant Marketing Authorisations to EGIS Pharmaceuticals Public Limited Company (PLC) for Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets on 10 February 2011. The Marketing Authorisations in the UK were granted on 14 March 2011.

The full PAR for Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets follows this summary.

For more information about treatment with Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in April 2015.
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I Introduction

Based on the review of the data on quality, safety and efficacy, Bulgaria (BG), the Czech Republic (CZ), Hungary (HU), Latvia (LV), Lithuania (LT), Poland (PL), Romania (RO), the Slovak Republic (SK) and the UK considered that the applications for Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets could be approved. Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are prescription only medicines (POM) and are indicated for the treatment of:

- Schizophrenia; olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response.
- Moderate to severe manic episode; in patients whose manic episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.

These applications for Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets were submitted according to Article 10(1) of Directive 2001/83/EC, as amended, referring to the innovator products Zyprexa 5 mg, 10 mg, 15 mg and 20 mg tablets (EU/1/96/022), first authorised in EEA on 27th September 1996 to Eli Lilly Nederland B.V.

The reference products are Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets, first authorised in the EEA to Eli Lilly Nederland B.V. on 3rd February 2000.

No new non-clinical studies were conducted, which is acceptable given that the products contain a widely-used, well-known active substance. No clinical studies, with the exception of the bioequivalence study, have been performed and none are required for these applications as the pharmacology of olanzapine is well-established.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the community, the RMS has accepted copies of current GMP Certificates or satisfactory inspection summary reports, ‘close-out letters’ or ‘exchange of information’ issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

The RMS considers that 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 satisfactory justification for non-submission of a Risk Management Plan has been provided.
II Quality aspects

II.1 Introduction
The applications were submitted according to Article 10(1) of Directive 2001/83/EC, as amended. The applicant has specified Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets as the UK reference medicinal product.

Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets are formulated as yellow to pale yellow, round, biconvex, orodispersible tablets and each tablet is embossed with ‘5’, ‘10’, ‘15’ and ‘20’, respectively, on one side.

Each Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablet contains 5 mg, 10 mg, 15 mg and 20 mg olanzapine, respectively.

The excipients present in the tablet core of each strength orodispersible tablet are: calcium carbonate DC CS90 (which consists of calcium carbonate, maize starch pregelatinised and maize starch), lactose monohydrate, crospovidone (Type A), aspartame (E951) and magnesium stearate.

The orodispersible tablets are presented in aluminium/peelable aluminium blisters, which are packed into cartons in pack sizes of 28, 30, 56, 60, 84 or 90 orodispersible tablets.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary product packaging complies with EU legislation regarding contact with food.

II.2 Drug Substance
INN/Ph.Eur name: Olanzapine
Chemical names:
- 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5] benzodiazepine

Structural formula:

![Structural formula of Olanzapine](image)

Molecular formula: \( C_{17}H_{20}N_4S \)

Appearance: Pale yellow to yellow powder.
Solubility: Freely soluble in chloroform, soluble in acetone, sparingly soluble in ethyl acetate and insoluble in water
Molecular weight: 312.44

Olanzapine complies with in-house specifications.
Synthesis of the drug substance from the designated starting materials has been adequately described, and appropriate in-process controls and intermediate specifications are applied.

Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data has been supplied for the active pharmaceutical ingredient. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance, with suitable test methods and limits. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all reference standards used.

Satisfactory specifications and Certificates of Analysis have been provided for all aspects of the container-closure system. A declaration has been provided that the primary packaging complies with current regulations concerning contact with foodstuff.

Adequate stability data have been generated showing the active substance to be a physically and chemically stable drug, and supporting an appropriate retest period.

II.3 Medicinal Product
Pharmaceutical development
The objective of the development programme was to produce safe, efficacious products containing olanzapine that could be considered generic medicinal products of Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets (Eli Lilly Nederland B.V.).

The applicant has provided suitable product development sections. Justifications for the use and amounts of each excipient have been provided and are valid.

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

The reference product used in the bioequivalence study is Zyprexa Velotab 5 mg orodispersible tablets, licensed in the EEA.

All excipients comply with their respective European Pharmacopoeia monographs.

None of the excipients used contain material of human origin.

The applicant has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as those intended for human consumption.

The supplier has confirmed that the magnesium stearate contained in this product is sourced from vegetable origin.

No genetically modified organisms (GMO) have been used in the preparation of these products.
Manufacture of the product
A satisfactory batch formula has been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. Process validation data on suitable sized batches of each strength product have been provided and are satisfactory. The applicant has committed to perform process validation on full commercial-scale batches of each strength post approval.

Product Specifications
The finished product specifications are acceptable. Test methods have been described and adequately validated, as appropriate. Batch analytical data have been provided and comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability of the product
Stability studies were performed on batches of the finished products in the packaging proposed for marketing and in accordance with current guidelines. These data support a shelf-life of 24 months with storage instructions ‘Store in original package in order to protect from moisture’. This is satisfactory.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The SmPCs, patient information leaflet (PIL) and labelling are pharmaceutically acceptable.

The Marketing Authorisation Application (MAA) forms are pharmaceutically satisfactory.

The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

It is recommended that Marketing Authorisations are granted for these applications.

III Non-clinical aspects
The pharmacodynamics, pharmacokinetics and toxicological properties of olanzapine are well-known. As olanzapine is a widely used, well-known active substance, the applicant has not provided any new non-clinical data and none are required.

The non-clinical overview has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

A satisfactory justification has been provided for non-submission of an Environmental Risk Assessment.

It is recommended that Marketing Authorisations are granted for these applications.

IV Clinical aspects
IV.1 Introduction
With the exception of the following bioequivalence study, no new pharmacokinetic or pharmacodynamic data were submitted with these applications and none were required.
IV.2 Pharmacokinetics
A randomised, single-dose, two-way, crossover study to compare the pharmacokinetics of the test product Olanzapine 5 mg orodispersible tablets versus the reference product Zyprexa Velotab (olanzapine) 5 mg tablets (Eli Lilly Nederland B.V.) in healthy subjects under fasted conditions.

Blood samples were taken pre-dose and up to 192 hours post dose. There was a washout period of 22 days between each treatment period. Pharmacokinetic parameters were calculated and statistically analysed.

Results for olanzapine are presented below as log-transformed values:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AUC_{0-t} (ng.h/mL)</th>
<th>AUC_{0-∞} (ng.h/mL)</th>
<th>C_{max} (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test (T)</td>
<td>256.047±50.5939</td>
<td>270.513±52.0186</td>
<td>8.160±1.6490</td>
</tr>
<tr>
<td>Reference (R)</td>
<td>270.303±55.3710</td>
<td>286.222±57.7112</td>
<td>8.547±1.7032</td>
</tr>
<tr>
<td>T/R Ratio (90% CI)</td>
<td>95.0</td>
<td>94.8</td>
<td>95.5</td>
</tr>
<tr>
<td></td>
<td>90.04 – 100.14</td>
<td>90.46 – 99.29</td>
<td>91.30 – 99.99</td>
</tr>
</tbody>
</table>

The results for the primary variables indicated that the 90% confidence intervals test/reference ratio of geometric means for AUC_{0-t} and C_{max} for olanzapine lie within acceptable limits (80-125%). Thus, bioequivalence has been shown between the test and reference products in this study.

The applicant adequately justified the use of the lower strength product for the bioequivalence study (5 mg) rather than the usual higher dose (20 mg). The 5 mg was selected on the basis of the higher doses having tolerability concerns. Considering that the pharmacokinetics of olanzapine are linear over the therapeutic range, the absorption is largely predictable and no food interaction is expected (fasted bioequivalence study) this is satisfactory.

As the 5 mg, 10 mg, 15 mg and 20 mg strength products meet all the criteria as specified in the Note for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 5 mg strength can be extrapolated to Olanzapine 10 mg, 15 mg and 20 mg orodispersible tablets.

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

IV.4 Clinical efficacy
No new efficacy data were submitted with these applications and none were required.

IV.5 Clinical safety
With the exception of the data submitted during the bioequivalence study, no new safety data were submitted with these applications and none were required. No new or unexpected safety concerns were raised during the bioequivalence study.

IV.6 Risk Management Plan (RMP)
A satisfactory justification for non-submission of a Risk Management Plan has been
V.7 Discussion on the clinical aspects
The SmPCs, PIL and labelling are medically satisfactory and consistent with those for the reference products, where appropriate.

The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

The MAA Forms are medically satisfactory.

It is recommended that Marketing Authorisations are granted for these applications.

V User consultation
The PIL has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended. The language used for the purpose of user testing the PIL was English.

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 important quality characteristics of Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible 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.

Efficacy
Bioequivalence has been demonstrated between the applicant’s Olanzapine 5 mg orodispersible tablets and the reference product Zyprexa Velotab 5 mg orodispersible tablets. These bioequivalence results and conclusions can be extrapolated to Olanzapine 10 mg, 15 mg and 20 mg orodispersible tablets.

No new or unexpected safety concerns arise from these applications.

The SmPCs, PIL and labelling are satisfactory and consistent with that for the reference products.

Benefit-risk assessment
The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with olanzapine is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
The Summary of Product Characteristics (SmPCs), PIL and labelling are satisfactory, in line with current guidelines and consistent with the reference products. In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPC and PIL for these products are available on the MHRA website.

The approved labelling texts are listed below:

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**Blistor Pack Carton**

1. **NAME OF THE MEDICINAL PRODUCT**

   Olanzapine 5 mg orodispersible tablets
   olanzapine

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

   Each orodispersible tablet contains 5 mg olanzapine.

3. **LIST OF EXCIPIENTS**

   Also contains: lactose monohydrate and aspartame (E951).
   See package leaflet for further information.

4. **PHARMACEUTICAL FORM AND CONTENTS**

   28 orodispersible tablets
   30 orodispersible tablets
   56 orodispersible tablets
   60 orodispersible tablets
   84 orodispersible tablets
   90 orodispersible tablets

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

   For oral use.
   Read the package leaflet before use.
   1. Carefully peel off the backing.
   2. Gently push the tablet out.
   3. Put the tablet in your mouth. It will dissolve directly in your mouth, so that it can be easily swallowed.

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

   Keep out of the reach and sight of children.
7. OTHER SPECIAL WARNING(S), IF NECESSARY.

8. EXPIRY DATE

Exp.: 

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORIZATION HOLDER

EGIS Pharmaceuticals PLC, 1106 Budapest, Keresztúri út 30-38, Hungary

12. MARKETING AUTHORIZATION NUMBER(S)

Reg. No.: PL 03525/0009

13. BATCH NUMBER

Batch: 

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

Use as directed by your doctor.

16. INFORMATION IN BRAILLE

Olanzapine 5 mg Orodispersible Tablets
MINIMUM PARTICULARS TO APPEAR ON BLISTERS

<table>
<thead>
<tr>
<th><strong>Blister</strong></th>
</tr>
</thead>
</table>

1. **NAME OF THE MEDICINAL PRODUCT**

Olanzapine 5 mg orodispersible tablets

olanzapine

2. **NAME OF THE MARKETING AUTHORISATION HOLDER**

EGIS

3. **EXPIRY DATE**

Exp

4. **BATCH NUMBER**

Batch:

5. **OTHER**
PARTICULARS TO APPEAR ON THE OUTER PACKAGING
Blister Pack Carton

1. NAME OF THE MEDICINAL PRODUCT

Olanzapine 10 mg orodispersible tablets
olanzapine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each orodispersible tablet contains 10 mg olanzapine.

3. LIST OF EXCIPIENTS

Also contains: lactose monohydrate and aspartame (E951).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 orodispersible tablets
30 orodispersible tablets
56 orodispersible tablets
60 orodispersible tablets
84 orodispersible tablets
90 orodispersible tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

1. Carefully peel off the backing.
2. Gently push the tablet out.
3. Put the tablet in your mouth. It will dissolve directly in your mouth, so that it can be easily swallowed.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY.

8. EXPIRY DATE

Exp.: 

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

EGIS Pharmaceuticals PLC, 1106 Budapest, Keresztúri út 30-38, Hungary

12. MARKETING AUTHORISATION NUMBER(S)

Reg. No.: PL 03525/0010

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

Use as directed by your doctor.

16. INFORMATION IN BRAILLE

Olanzapine 10 mg Orodispersible Tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

Blister

1. NAME OF THE MEDICINAL PRODUCT

Olanzapine 10 mg orodispersible tablets

olanzapine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

EGIS

3. EXPIRY DATE

Exp

4. BATCH NUMBER

Batch:

5. OTHER
PARTICULARS TO APPEAR ON THE OUTER PACKAGING
Blister Pack Carton

1. NAME OF THE MEDICINAL PRODUCT

Olanzapine 15 mg orodispersible tablets
olanzapine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each orodispersible tablet contains 15 mg olanzapine.

3. LIST OF EXCIPIENTS

Also contains: lactose monohydrate and aspartame (E951).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 orodispersible tablets
30 orodispersible tablets
56 orodispersible tablets
60 orodispersible tablets
84 orodispersible tablets
90 orodispersible tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

1. Carefully peel off the backing.
2. Gently push the tablet out.
3. Put the tablet in your mouth. It will dissolve directly in your mouth, so that it can be easily swallowed.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY.

8. EXPIRY DATE

Exp.:

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture
10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

EGIS Pharmaceuticals PLC, 1106 Budapest, Keresztúri út 30-38, Hungary

12. MARKETING AUTHORISATION NUMBER(S)

Reg. No.: PL 03525/0011

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

Use as directed by your doctor.

16. INFORMATION IN BRAILLE

Olanzapine 15 mg Orodispersible Tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

Blister

1. NAME OF THE MEDICINAL PRODUCT

Olanzapine 15 mg orodispersible tablets

olanzapine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

EGIS

3. EXPIRY DATE

Exp

4. BATCH NUMBER

Batch:

5. OTHER
1. NAME OF THE MEDICINAL PRODUCT

Olanzapine 20 mg orodispersible tablets
olanzapine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each orodispersible tablet contains 20 mg olanzapine.

3. LIST OF EXCIPIENTS

Also contains: lactose monohydrate and aspartame (E951).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

28 orodispersible tablets
30 orodispersible tablets
56 orodispersible tablets
60 orodispersible tablets
84 orodispersible tablets
90 orodispersible tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

1. Carefully peel off the backing.
2. Gently push the tablet out.
3. Put the tablet in your mouth. It will dissolve directly in your mouth, so that it can be easily swallowed.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY.

8. EXPIRY DATE

Exp.:

9. SPECIAL STORAGE CONDITIONS
Store in the original package in order to protect from moisture

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORITY

EGIS Pharmaceuticals PLC, 1106 Budapest, Keresztúri út 30-38, Hungary

12. MARKETING AUTHORITY NUMBER(S)

Reg. No.: PL 03525/0012

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

Use as directed by your doctor.

16. INFORMATION IN BRAILLE

Olanzapine 20 mg Orodispersible Tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

Blister

1. NAME OF THE MEDICINAL PRODUCT

Olanzapine 20 mg orodispersible tablets

olanzapine

2. NAME OF THE MARKETING AUTHORITY

EGIS

3. EXPIRY DATE

Exp

4. BATCH NUMBER

Batch:

5. OTHER
Table of content of the PAR update for MRP and DCP
Steps taken after the initial procedure with an influence on the Public Assessment Report
(Type II variations, PSURs, commitments)

<table>
<thead>
<tr>
<th>Scope</th>
<th>Procedure number</th>
<th>Product information affected</th>
<th>Date of start of the procedure</th>
<th>Date of end of procedure</th>
<th>Approval / non approval</th>
<th>Assessment report attached Y/N (version)</th>
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<td>To update the SmPC and PIL in line with the reference product and QRD template</td>
<td>UK/H/4082/001-004/IB/007</td>
<td>Y</td>
<td>18 February 2015</td>
<td>11 March 2015</td>
<td>Approval</td>
<td>Y</td>
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Annex 1


Product:  Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets

Marketing Authorisation Holder:  EGIS Pharmaceuticals PLC.

Active Ingredient:  Olanzapine

Reason:
To update sections 4.2 (Posology and method of administration), 4.4 (Special warnings and precautions for use), 4.6 (Fertility, pregnancy and lactation), 4.8 (Undesirable effects), 5.1 (Pharmacodynamic properties) and 5.2 (Pharmacokinetic properties) of the SmPC and consequentially the leaflet in line with the reference product and Quality Review of Documents (QRD) template.

Supporting Evidence
Updated sections 4.2, 4.4, 4.6, 4.8, 5.1 and 5.2 of the SmPC and an updated version of the package leaflet were submitted.

Evaluation
The SmPCs for Olanzapine 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets have been updated in line with that as approved for the reference products, Zyprexa Velotab 5 mg, 10 mg, 15 mg and 20 mg orodispersible tablets and are acceptable.

Consequential updates to the package leaflet are also acceptable.

Conclusion
The amendments to the SmPC fragments and the package leaflet can be approved.

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) for products granted marketing authorisations at a national level are available on the Medicines and Healthcare products Regulatory Agency website.

Decision - Approved
Date 11 March 2015