Mirtazapine 15 mg orodispersible tablets
Mirtazapine 30 mg orodispersible tablets
Mirtazapine 45 mg orodispersible tablets

PL 40378/0022-0024

UKPAR

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This is a summary of the public assessment report (PAR) for Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets. It explains how the products 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 Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets. These medicinal products will be collectively referred to as Mirtazapine orodispersible tablets in the remainder of this summary.

For practical information about using Mirtazapine orodispersible tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Mirtazapine orodispersible tablets and what are they used for?
These medicines are the same as the Mirtazapine 15mg, 30mg and 45mg Orodispensible Tablets marketed by Actavis Group PTC ehf (PL 30306/0368-0370). Actavis Group PTC ehf. agreed that these marketing authorisations can be used as a basis for the grant of identical marketing authorisations for Mirtazapine orodispersible tablets (informed consent).

Mirtazapine orodispersible tablets are used to treat depressive illness.

How do Mirtazapine orodispersible tablets work?
Mirtazapine belongs to a group of medicines called the antidepressants. Mirtazapine affects the levels of certain chemicals in the brain that may become unbalanced and cause depression.

How are Mirtazapine orodispersible tablets used?
The usual starting dose is 15 or 30 mg every day. A doctor may advise an increase in dose after a few days to the amount that may be best for the patient (between 15 and 45 mg per day). The dose is usually the same for all ages. However, elderly people or patients with renal or liver disease may be advised to take a different dose by the doctor.
Mirtazapine orodispersible tablets should be taken at the same time each day and are best taken as a single dose before the patient goes to bed. However a doctor may suggest for the dose to be split – once in the morning and once at night-time before the patient goes to bed. The higher dose should be taken by the patient before they go to bed.

This medicine can only be obtained with a prescription.

**What benefits of Mirtazapine orodispersible tablets have been shown in studies?**
Mirtazapine orodispersible tablets are considered to be identical to previously authorised Mirtazapine 15mg, 30mg and 45mg Orodispersible Tablets, with the same benefits and risks. Therefore, no new studies have been provided for Mirtazapine orodispersible tablets but reference is made to the Marketing Authorisations for Mirtazapine 15mg, 30mg and 45mg Orodispersible Tablets.

**What are the possible side effects from Mirtazapine orodispersible tablets?**
The most common side effects with Mirtazapine orodispersible tablets, which may affect more than 1 in 10 people, are increase in appetite and weight gain, drowsiness or sleepiness, headache and dry mouth.

For the full list of all side effects reported with Mirtazapine orodispersible tablets, see section 4 of the package leaflet. For the full list of restrictions, see the package leaflet.

**Why are Mirtazapine orodispersible tablets approved?**
The MHRA decided that the benefits of Mirtazapine orodispersible tablets are greater than their risks and recommended that they be approved for use.

**What measures are being taken to ensure the safe and effective use of Mirtazapine orodispersible tablets?**
A Risk Management Plan has been developed to ensure Mirtazapine orodispersible tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Mirtazapine orodispersible tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

**Other information about Mirtazapine orodispersible tablets**
A Marketing Authorisation was granted in the UK on 30 September 2014.

This summary was last updated in December 2014.

The full PAR for Mirtazapine orodispersible tablets follows this summary.
MIRTAZAPINE 15 MG ORODISPERSIBLE TABLETS
MIRTAZAPINE 30 MG ORODISPERSIBLE TABLETS
MIRTAZAPINE 45 MG ORODISPERSIBLE TABLETS

PL 40378/0022-0024

SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Aptil Pharma Limited Marketing Authorisations for the medicinal products Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets (PL 40378/0022-0024) on 30 September 2014.

Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets are indicated in adults for the treatment of episodes of major depression.

These applications were submitted as abridged applications, according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to the Marketing Authorisations for Mirtazapine 15mg, 30mg and 45mg Orodispersible Tablets (PL 30306/0368-0370) which were licensed to Actavis Group PTC ehf. on 13 July 2011. Mirtazapine 15mg, 30mg and 45mg Orodispersible Tablets were originally licensed to Olinka UK Limited on 24 July 2007 (PL 08608/0117-0119). The Marketing Authorisations were then transferred to Medis EHF on 16 January 2008 (PL 24702/0069-71) before the change of ownership to Actavis Group PTC ehf.

Mirtazapine is a centrally active presynaptic α2-antagonist, which increases central noradrenergic and serotonergic neurotransmission. The enhancement of serotonergic neurotransmission is specifically mediated via 5-HT1 receptors, because 5-HT2 and 5-HT3 receptors are blocked by mirtazapine. Both enantiomers of mirtazapine are presumed to contribute to the antidepressant activity, the S(+) enantiomer by blocking α2 and 5-HT2 receptors and the R(-) enantiomer by blocking 5-HT3 receptors.

The histamine H1-antagonistic activity of mirtazapine is responsible for its sedative properties. It has practically no anticholinergic activity and, at therapeutic doses, has practically no effect on the cardiovascular system.

No new data were submitted nor were necessary for these simple applications, as the data are identical to those provided for the previously authorised products.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 40378/0022-0024
PROPRIETARY NAME: Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets
ACTIVE: Mirtazapine
COMPANY NAME: Aptil Pharma Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS: POM

1. INTRODUCTION
These are abridged applications for Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets, submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Mirtazapine 15mg, 30mg and 45mg Orodispersible Tablets (PL 30306/0368-0370). The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name
The name of the products is acceptable.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The tablets have the same strengths, form and route of administration as the reference products.

Mirtazapine 15 mg, 30 mg and 45 mg orodispersible tablets are stored in:

1. Al/Al Blister, pack sizes; 5, 6, 7, 10, 14, 15, 20, 21, 28, 30, 50, 56, 60, 84, 90, 98 and 100 Tablets.
2. Al/Al Blister with peel off foil, pack sizes; 5, 6, 7, 10, 14, 15, 20, 21, 28, 30, 50, 56, 60, 84, 90, 98 and 100 Tablets.
3. PP securitainers, pack sizes; 5, 6, 7, 10, 14, 15, 20, 21, 28, 30, 50, 56, 60, 84, 90, 98 and 100 Tablets.
4. HDPE containers with LDPE caps, pack sizes; 5, 6, 7, 10, 14, 15, 20, 21, 28, 30, 50, 56, 60, 84, 90, 98 and 100 Tablets.

2.3 Legal status
The tablets are only available with a prescription.

2.4 Marketing Authorisation Holder
The Marketing Authorisation Holder is Aptil Pharma Limited, 9th Floor, CP House, 97-107 Uxbridge Road, Ealing, London W5 5TL, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.
2.5 Manufacturers
The manufacturing sites are identical to those of the reference products and are acceptable.

2.6 Qualitative and quantitative composition
The products’ compositions are identical to those of the reference products and are acceptable.

2.7 Manufacturing process
The manufacturing process is identical to that of the reference products and is acceptable.

2.8 Finished product/shelf-life specification
The finished product specifications are identical to those of the reference products and are acceptable.

2.9 Drug substance specification
The drug substance specification is identical to that of the reference products and is acceptable.

2.10 TSE Compliance
Not applicable

2.11 Bioequivalence
No bioequivalence data are required to support these simple abridged applications because the products are identical to products that are already authorised.

3. EXPERT REPORTS
These are acceptable.

4. PRODUCT NAME AND APPEARANCE
The names and appearance of the products are identical to those of the reference products and are acceptable.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The Summaries of Product Characteristics are identical to those of the reference products, apart from the necessary administrative updates to reflect the change in Marketing Authorisations, and are acceptable.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
The PIL and labels are identical to those of the reference product, apart from the necessary administrative updates to reflect the change in Marketing Authorisations, and are acceptable.

7. CONCLUSION
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA).

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Risk Management Plan is considered adequate. Routine risk minimisation is provided through the Summaries of Product Characteristics and the Patient Information Leaflet and this is sufficient.

The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with the data previously assessed for the Marketing Authorisation for Mirtazapine 15mg, 30mg and 45mg Orodispersible Tablets (PL 30306/0368-0370) and, as such, have been judged to be satisfactory.

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

EFFICACY
The products are identical to those previously licensed; therefore, no efficacy data are needed.

SAFETY
No new or unexpected safety concerns arose from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labels are identical to those previously approved, apart from the necessary administrative updates to reflect the change in Marketing Authorisations.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the reference products. The benefit/risk balance is therefore considered to be positive.
MIRTAZAPINE 15 MG ORODISPERSIBLE TABLETS
MIRTAZAPINE 30 MG ORODISPERSIBLE TABLETS
MIRTAZAPINE 45 MG ORODISPERSIBLE TABLETS

PL 40378/0022-0024

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 21 January 2013.

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 2 May 2013.

3 Following assessment of the application the MHRA requested further information relating to the dossier on 14 August 2013 and 19 May 2014.

4 The applicant responded to the MHRA’s request, providing further information on 15 February 2014, 25 June 2014 and 17 September 2014.

5 The application was granted on 30 September 2014.
# STEPS TAKEN AFTER INITIAL AUTHORISATION – SUMMARY

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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.
LABELLING

Mirtazapine 15 mg orodispersible tablets

Blister:
Mirtazapine 30 mg orodispersible tablets

Blister:
Mirtazapine 45 mg orodispersible tablets

Blister: