EBESQUE XL 50 MG PROLONGED-RELEASE TABLETS
PL 20311/0026
EBESQUE XL 200 MG PROLONGED-RELEASE TABLETS
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UKPAR

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LAY SUMMARY

This is a summary of the Public Assessment Report (PAR) for Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets (PL 20311/0026-0029). It explains how Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets were assessed and their authorisations recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

For practical information about using Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets and what are they used for?
Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets contain the active substance quetiapine (as quetiapine fumarate). These tablets belong to a group of medicines known as anti-psychotics and can be used to treat several illnesses, such as schizophrenia, mania and bipolar depression.

These medicines are identical to Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 20658/0076 and PL 20658/0078-0080), which were authorised to Torrent Pharma GmbH on 27 July 2011. Following a subsequent change of ownership procedure, the current marketing authorisation holder for Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets, since 28 August 2012, has been Torrent Pharma (UK) Limited (PL 36687/0062-0065).

How are Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets used?
Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets are prescription-only medicines (legal status POM). Depending on the illness and the needs of the patient, the daily dose will usually be between 150 and 800 mg and the medicine is taken as single dose, swallowed with water, without food, and at least an hour before a meal or at bedtime.

Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets are for use only in adults and adolescents aged 18 years and above. Details of the correct dose to be given will be provided by the prescribing doctor.

How do Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets work?
The active substance, quetiapine, is an antipsychotic drug. Quetiapine is converted, in the body, into another compound, norquetiapine. Both of these substances have a strong blocking action on specific signalling pathways within the brain. It is believed that this blocking action is responsible for the clinical antipsychotic effect of these medicines.

How have Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets been studied?
Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets are identical to the previously granted marketing authorisations for Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 36687/0062-0065). The current marketing authorisation holder, Torrent Pharma (UK) Limited, has agreed that scientific data presented for Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 36687/0062-0065) can be used for these applications for Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets.

What are the benefits and risks of Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets?
As Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets (PL 20311/0026-0029) are considered identical to Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 36687/0062-0065) their benefits and risks are taken as being the same as those for Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 36687/0062-0065).

Why are Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets approved?
No new or unexpected safety concerns arose from these applications. It was, therefore, considered that the benefits of Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets outweigh their risks, and the grant of these Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets?
A risk management plan has been developed to ensure that Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release 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 Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets
The Marketing Authorisations were granted in the UK on 28 July 2014.

For more information about taking Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in August 2014.

The full PAR for Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets follows this summary.

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations to Dallas Burston Ashbourne Limited for the medicinal products Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets (PL 20311/0026-0029) on 28 July 2014. These are prescription-only medicines (legal status POM) and are used to treat:

- Schizophrenia, including preventing relapse in stable schizophrenic patients who have been maintained on Ebesque XL
- Bipolar disorder (specifically the treatment of moderate to severe manic episodes, major depressive episodes, and the prevention of recurrence in patients who have responded to quetiapine treatment)
- Major depressive episodes, as an add-on treatment in patients with Major Depressive Disorder (MDD) who have had sub-optimal response to antidepressant monotherapy.

These applications were submitted as abridged simple applications according to Article 10c of Directive 2001/83/EC, as amended. The applications cross-refer to Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 36687/0062-0065) which were granted to the current marketing authorisation holder, Torrent Pharma (UK) Limited, on 28 August 2012. (These marketing authorisations were originally granted to Torrent Pharma GmbH on 27 July 2011 (PL 20658/0076 and PL 20658/0078-0080), but subsequently underwent a change of ownership to Torrent Pharma (UK) Limited).

These medicinal products contain the active substance quetiapine (as quetiapine fumarate), which is broken down in the body to another compound, norquetiapine. Both of these substances have strong and selective inhibitory action on brain serotonin ($5HT_2$) and dopamine D_1- and D_2 receptors. A combination of inhibitory action at these receptors, with a higher selectivity for the $5HT_2$ receptors compared with the D_2- receptors, is believed to be responsible for the clinical antipsychotic effect of these medicines.

PHARMACEUTICAL ASSESSMENT

LICENCE NUMBERS:	PL 20311/0026-0029
PROPRIETARY NAMES:	Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets
ACTIVE:	Quetiapine fumarate
COMPANY NAME:	Dallas Burston Ashbourne Ltd
E.C. ARTICLE:	Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS:	POM

1. INTRODUCTION

These are simple, piggyback (informed consent) applications for Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets, submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed MA holder is Dallas Burston Ashbourne Ltd, The Rectory, Braybrooke Road, Arthingworth, Market Harborough, LE16 8JT, UK.

The applications cross-refer to licences for Quettor XL 50mg, 200mg, 300mg and 400mg Prolonged Release Tablets (PL 36687/0062-0065) which were granted to the current marketing authorisation holder, Torrent Pharma (UK) Limited, on 28 August 2012. (These marketing authorisations were originally granted to Torrent Pharma GmbH on 27 July 2011 (PL 20658/0076 and PL 20658/0078-0080), but subsequently underwent a change of ownership to Torrent Pharma (UK) Limited).

The applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed names of the products are Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablets. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Each Ebesque XL 50, 200, 300 and 400 mg Prolonged-Release Tablet contains 50, 200, 300 and 400 mg of quetiapine (as quetiapine fumarate), respectively.

The tablets are packaged in either polyvinylchloride/polyvinylidene chloride/aluminium blisters or oriented polyamide/aluminium/polyvinylchloride blisters, both contained in cardboard cartons, in pack sizes of 10, 50, 60 and 100 prolonged-release tablets.

The proposed shelf-life for the Ebesque XL 50 mg Prolonged-Release Tablets is 27 months and the storage conditions are “Do not store above 30°C”. The proposed shelf-life of the Ebesque XL 200, 300 and 400 mg Prolonged-Release Tablets is 36 months and there are no special storage conditions. These are consistent with the details registered for the cross-reference products.

2.3 Legal status

On approval, these products will be available as prescription-only medicines (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Dallas Burston Ashbourne Ltd, The Rectory, Braybrooke Road, Arthingworth, Market Harborough, LE16 8JT, UK.

The QP responsible for pharmacovigilance is stated and their 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 compositions are 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.

2.8 Finished product/shelf-life specification

The proposed finished product specifications are 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

The suppliers of lactose monohydrate have confirmed that the lactose is collected under the same conditions as milk for human consumption. This is consistent with the cross-reference products.

3. EXPERT REPORTS

The applicant has included detailed expert reports in Module 2 of the applications. 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 Section 2.1 for details of the proposed product names. The appearances of the products are 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 Label

The proposed artwork is comparable with the artwork registered for the cross-reference products and complies with statutory requirements. The applicant has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with the 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 BENEFIT-RISK ASSESSMENT

QUALITY
The data for these applications are consistent with that assessed for the cross-reference products and as such has been judged to be satisfactory.

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 arose from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory.

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 quetiapine fumarate is considered to have demonstrated the therapeutic value of the compound. The benefit-risk assessment is therefore considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 15 October 2013.
2	Following standard checks and communication with the applicant, the MHRA considered the applications valid on 30 October 2013.
3	Following assessment of the applications, the MHRA requested further information relating to the dossiers on 27 January 2014, 04 April 2014 and 19 June 2014.
4	The applicant responded to the MHRA's requests, providing further information on 25 February 2014, 16 May 2014 and 25 June 2014.
5	The applications were determined on 28 July 2014.

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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

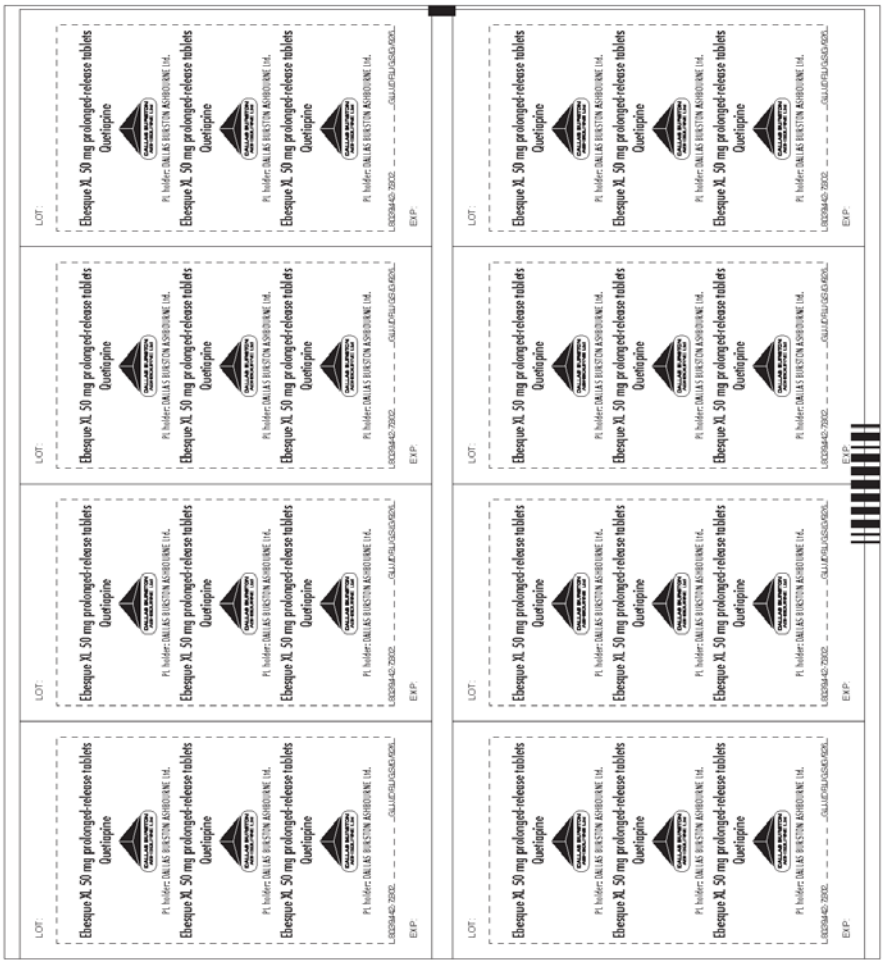
Date submitted	Application type	Scope	Outcome

Summary of Product Characteristics and Patient Information Leaflet

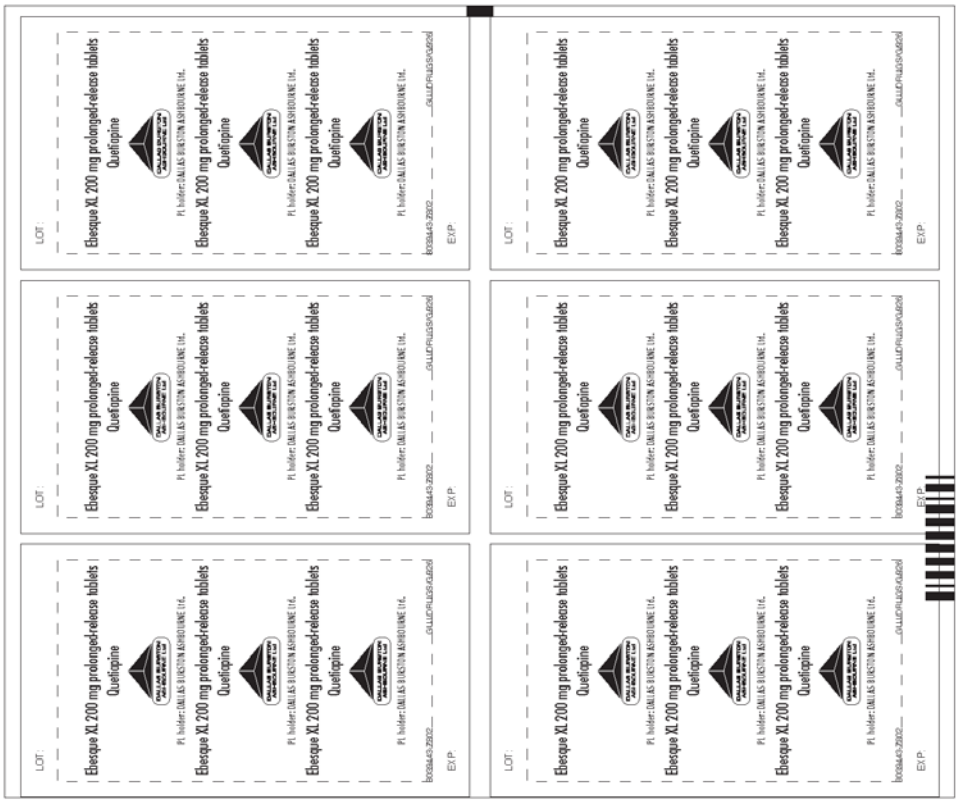
In accordance with Directive 2012/84/EU, the current approved UK versions of the Summaries of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) for these products are available on the MHRA website.

Labelling

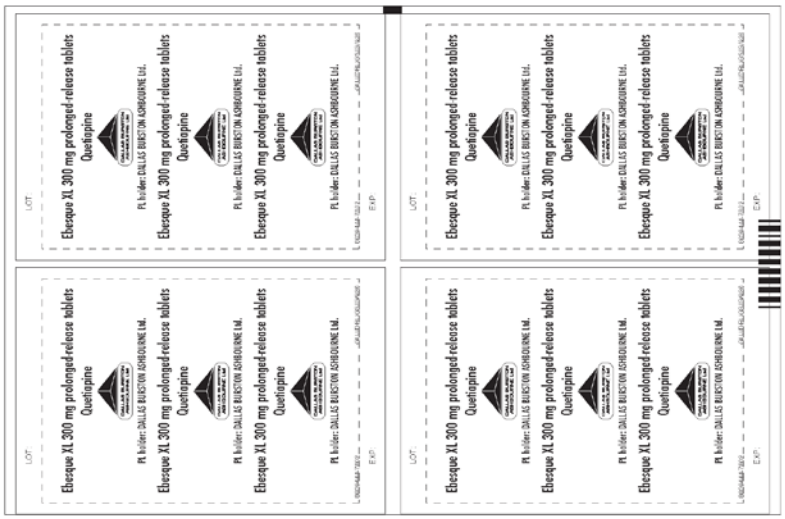
50 mg Carton and Label


LOT:
Ebesque XL 50 mg prolonged-release tablets
Quetiapine
PL holder: DALLAS BURSTON ASHBOURNE Ltd.
EXP:

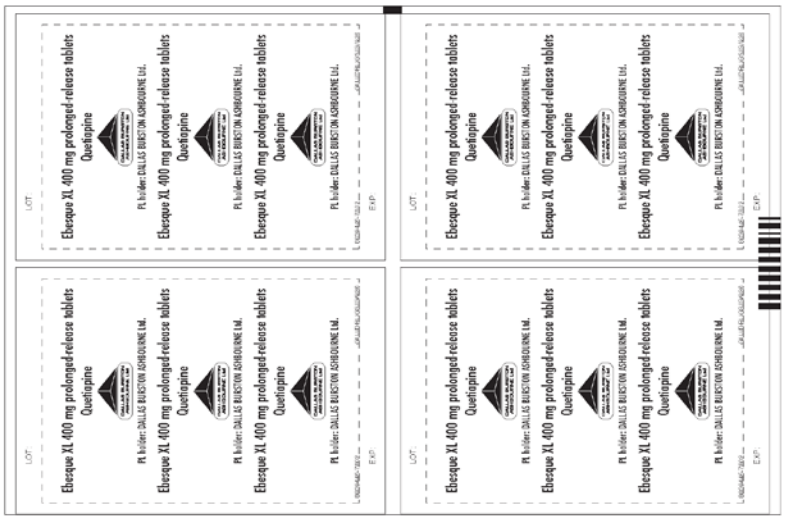
200 mg Carton and Label


LOT:
Ebesque XL 200 mg prolonged-release tablets
Quetiapine
PL holder: DAILAS BIOKSTIN ASHDURNE Ltd.
EXP:

300 mg Carton and Label


LOT
Ebesque XL 300 mg prolonged-release tablets
Quetiapine
PL holder: DALLAS BIOESTON AGROQUIMICA Ltd.
EXP

400 mg Carton and Label


LOT
Ebesque XL 400 mg prolonged-release tablets
Quetiapine
PL holder: DALLAS BIOESTON ADRODERNE Ltd.
EXP