Public Assessment Report

Decentralised Procedure

Trazodone Hydrochloride 50 mg tablets
Trazodone Hydrochloride 100 mg tablets
Trazodone Hydrochloride 150 mg tablets

(Trazodone hydrochloride)

Procedure No: UK/H/6352/001-003/DC

UK Licence Number: PL 20075/0495-0497

Accord Healthcare Limited
LAY SUMMARY

Trazodone Hydrochloride 50 mg tablets
Trazodone Hydrochloride 100 mg tablets
Trazodone Hydrochloride 150 mg tablets

This is a summary of the Public Assessment Report (PAR) for Trazodone Hydrochloride 50 mg, 100 mg and 150 mg tablets (PL 20075/0495-0497; UK/H/6352/001-003/DC). It explains how Trazodone Hydrochloride 50 mg, 100 mg and 150 mg 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 Trazodone Hydrochloride 50 mg, 100 mg and 150 mg tablets.

The product will be referred to as ‘Trazodone Tablets’ throughout the remainder of this public assessment report (PAR).

For practical information about using Trazodone Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Trazodone Tablets and what are they used for?
Trazodone Tablets are ‘generic medicines’. This means that Trazodone hydrochloride Tablets are similar to ‘reference medicines’ already authorised in the European Union (EU) called Molipaxin 50mg capsules/Trazodone hydrochloride 50mg capsules, Molipaxin 100mg Capsules/Trazodone hydrochloride 100mg Capsules and Molipaxin 150mg Tablets/Trazodone hydrochloride 150mg Tablets (Winthrop Pharmaceuticals UK Limited). The reference medicine will be referred to as ‘Molipaxin 50mg/100mg Capsules and Molipaxin 150mg Tablets’ throughout the remainder of this public assessment report (PAR).

Trazodone Tablets can be used to treat symptoms of depression (major depressive episodes).

How do Trazodone Tablets work?
This medicine contains the active substance called trazodone hydrochloride. This belongs to a group of medicines called antidepressants. It affects chemicals in the brain that may be unbalanced in people with depression.

How are Trazodone Tablets used?
The pharmaceutical form of this medicine is a tablet and the route of administration is oral (by mouth). The 100 mg and 150 mg tablets can be divided into equal doses. For the 50 mg strength tablet; the score line is not intended breaking the tablet.

The patient should always take this medicine exactly as their doctor or pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

The recommended dose is:

Adults:
Depression
- Adults usually start by taking 150 mg each day in a single or divided dose
- The patient’s doctor may increase the dose every 3-4 days by steps of 50 mg up to a maximum of 300 mg each day depending on their condition.
- For adults in hospital the dose may be as high as 600mg each day.
Elderly
- Older people or those who are frail will usually be given a starting dose of 100mg each day.

Children and adolescents
Children and adolescents under 18 years should not take Trazodone Tablets.

Taking this medicine
- The patient should swallow the tablet with a drink of water
- This medicine can be taken after food. This will help lower the chances of side effects.
- If the patient has been told to take this medicine only once each day then they should take it before going to bed
- If the patient feels the effect of this medicine is too weak or strong, the patient should not change the dose themselves but ask their doctor.

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

For further information on how Trazodone Tablets are used, refer to the package leaflet and Summaries of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

Trazodone Tablets can only be obtained with a prescription.

What benefits of Trazodone Tablets have been shown in studies?
Because Trazodone Tablets are generic medicines and are bioequivalent to the reference medicines Molipaxin 50mg/100mg Capsules and Molipaxin 150mg Tablets (Winthrop Pharmaceuticals UK Limited), its benefits and risks is taken as being the same as those of the reference medicine.

What are the possible side effects of Trazodone Tablets?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

For a full list of all the side effects reported with Trazodone Tablets see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

For the full list of restrictions, see the package leaflet.

Why are Trazodone Tablets approved?
It was concluded that, in accordance with EU requirements, Trazodone Tablets have been shown to have comparable quality and to be bioequivalent to Molipaxin 50mg/100mg Capsules and Molipaxin 150mg Tablets (Winthrop Pharmaceuticals UK Limited), that their benefits are greater than the risks and it was recommended that Trazodone Tablets can be approved for use.

What measures are being taken to ensure the safe and effective use of Trazodone Tablets?
A risk management plan (RMP) has been developed to ensure that Trazodone Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics (SmPC) and the package leaflet for Trazodone 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 Trazodone Tablets
Ireland, Italy, The Netherlands, and the UK agreed to grant marketing authorisations for Trazodone Hydrochloride 50 mg tablets and Trazodone Hydrochloride 150 mg tablets on 04 April 2018.

Germany, Ireland, Italy, Spain, The Netherlands, and the UK agreed to grant a marketing authorisation for Trazodone hydrochloride 100 mg tablets on 04 April 2018.

Following a subsequent national phase, a marketing authorisation was granted in the UK on 02 May 2018.

The full PAR for Trazodone Tablets follows this summary.

For more information about treatment with Trazodone Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in July 2018.
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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Accord Healthcare Limited, marketing authorisations for the medicinal products Trazodone Tablets (PL 20075/0495-0497; UK/H/6352/001-003/DC). Trazodone Tablets are a prescription-only medicine (POM).

Trazodone Tablets are indicated for major depressive episodes.

These applications were submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS) and Ireland, Italy and The Netherlands as a Concerned Member States (CMS) for Trazodone Hydrochloride 50 mg and Trazodone Hydrochloride 150 mg tablets (PL 20075/0495 and 0497; UK/H/6352/001and 003/DC) and Germany, Ireland, Italy, Spain, The Netherlands as CMS’ for Trazodone Hydrochloride 100 mg tablets (PL 20075/0496; UK/H/6352/002/DC). These applications were submitted under Article 10(1) of Directive 2001/83/EC, as amended, as generic applications.

The reference products for these applications are Molipaxin 50mg capsules/Trazodone hydrochloride 50mg capsules, Molipaxin 100mg Capsules/Trazodone hydrochloride 100mg Capsules and Molipaxin 150mg Tablets/Trazodone hydrochloride 150mg Tablets, which were first authorised to the marketing authorisation holder (MAH) Roussel Laboratories Limited (PL 00109/0045-0046 and PL 00109/0133) on 11 July 1980 and 08 May 1989 respectively. Molipaxin 50mg capsules/Trazodone hydrochloride 50mg capsules and Molipaxin 100mg Capsules/Trazodone hydrochloride 100mg Capsules subsequently underwent change of ownership procedures to Aventis Pharma Limited (PL 04425/0609 and 04425/0180) on 26 August 2009. Following further change of ownership procedures, marketing authorisation was granted to the current MAH; Winthrop Pharmaceuticals UK Limited (PL 17780/0616 and PL 17780/0618) on 17 September 2012.

Molipaxin 150 mg Tablets/ Trazodone Hydrochloride 150mg Tablets underwent a subsequent change of ownership procedure, to Aventis Pharma Limited, UK (PL 04425/0606) on 30 January 2010. Following a further change of ownership procedure, a marketing authorisation was granted to the current marketing authorisation holder (MAH) Winthrop Pharmaceuticals UK Limited (PL 17780/0616) on 05 November 2012. The reference medicine used to establish bioequivalence of Trazodone Tablets was Molipaxin 100 mg Capsules and Molipaxin 150 mg Tablets (Winthrop Pharmaceuticals UK Limited; PL 17780/0618 and PL 17780/0616).

Trazodone is a triazolopyridine derivative which differs chemically from other currently available antidepressants. Although trazodone bears some resemblance to the benzodiazepines, phenothiazines and tricyclic antidepressants, its pharmacological profile differs from each of these classes of drugs. It has negligible effect on noradrenaline re-uptake mechanisms. Whilst the mode of action of trazodone hydrochloride is not known precisely, its antidepressant activity may concern noradrenergic potentiation by mechanisms other than uptake blockade. A central antiserotonin effect may account for the drug’s anxiety reducing properties.

No new non-clinical studies were submitted, which is acceptable given that these applications were based on being a generic medicinal product of a reference product that has been in clinical use for over 10 years.

Two bioequivalence studies in healthy volunteers were submitted to support this application. The applicant has stated that the bioequivalence studies were conducted in accordance with Good Clinical Practice (GCP).
The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture, assembly and batch release of these products.

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.

The RMS considered that these applications could be approved at the end of procedure on 04 April 2018. After a subsequent national phase, a licence was granted in the UK on 02 May 2018.
II QUALITY ASPECTS

II.1 Introduction
The finished product is formulated as a tablet containing 50, 100 and 150 mg trazodone hydrochloride per tablet. Other ingredients consist of the pharmaceutical excipients Cellulose, microcrystalline, sodium starch glycolate (Type A), Starch, pregelatinised (maize), Silica, colloidal anhydrous and Magnesium stearate.

Trazodone Tablets are packaged in the following container materials:
- Aluminium/ oriented polyamide and polyvinyl chloride (OPA-Aluminium-PVC)
- Aluminium/ polyvinyl chloride and polyvinylidene chloride (Aluminium, PVC-PVdC)
- Aluminium/ polyvinyl chloride (Aluminium, PVC)

Trazodone Tablets are available in following pack sizes:
- 50 mg: 30 or 84 tablets in blister. Also available in 84 x 1 perforated unit dose blister.
- 100 mg: 20, 30, 50, 56, 60 or 100 tablets in blister. Also available in 56 x 1 perforated unit dose blister.
- 150 mg: 28 tablets in blister. Also available in 28 x 1 perforated unit dose blister.

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.

II.2 Drug Substance

INN: Trazodone hydrochloride
Chemical name: 2-[3-[4-(m-Chlorophenyl)-1-piperazinyl]propyl]s-triazolo[4,3-a]pyridin-3(2H)-one monohydrochloride

Structure:

![Trazodone Hydrochloride structure](image)

Molecular formula: C_{19}H_{22}ClN_{5}O, HCl
Molecular weight: 408.3 g/mol
Appearance: White or almost white, crystalline powder
Solubility: Soluble in water, sparingly soluble in ethanol (96%); practically insoluble in ether.

The drug substance, trazodone hydrochloride is the subject of an active substance master file (ASMF).

Synthesis of the active 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 have been supplied for the active substance. All potential known impurities have been identified and characterised.
An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analyses data are provided that comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards used.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3. Medicinal Product Pharmaceutical Development

The objective of the development programme was to develop safe, efficacious, tablets containing 50 mg, 100 mg and 150 mg trazodone hydrochloride per tablet that are generic versions of the reference products Molipaxin 50mg/100mg Capsules and Molipaxin 150mg Tablets (Winthrop Pharmaceuticals UK Limited). The development of the products has been described, the choice of excipients is justified, and their functions explained.

Comparative in vitro dissolution profiles have been provided for the proposed and reference product, similarity has been confirmed between the two.

All excipients comply with their respective European Pharmacopeia monographs. Satisfactory specifications and Certificates of Analysis have been provided for the packaging components.

None of the excipients used contain material of animal or human origin.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product

Satisfactory batch formulae have been provided for the manufacture of the product, together with an appropriate account of the manufacturing process. Process validation data on commercial size batches have been provided. The results are satisfactory.

Finished Product Specification

The finished product specification proposed is acceptable. Test methods have been described that have been adequately validated. Batch data complying with the release specification have been provided. Certificates of Analysis have been provided for all working standards used.

Stability of the Product

Finished product stability studies were performed in accordance with current guidelines on batches of the finished product in the packaging proposed for marketing. The data from these studies support a shelf-life of 2 years with the storage conditions ‘Store in the original package in order to protect from light’. Trazodone Tablets do not require any special temperature storage conditions.

Suitable post approval stability commitments to continue stability testing on batches of finished product have been provided.

II.4 Discussion on chemical, pharmaceutical and biological aspects

There are no objections to the approval of this application from a pharmaceutical viewpoint.
III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of trazodone hydrochloride are well-known, no new non-clinical studies are required and none have been provided. An overview based on the literature review is, thus, appropriate.

The applicant’s non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2 Pharmacology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.3 Pharmacokinetics
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.4 Toxicology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)
Since Trazodone Tablets are intended for generic substitution, this will not lead to an increase of the environment exposure. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects
There are no objections to the approval of this application from a non-clinical viewpoint.

IV CLINICAL ASPECTS

IV.1 Introduction
The pharmacodynamic, pharmacokinetic, clinical efficacy and safety properties of trazodone hydrochloride are well known. A comprehensive review of the published literature has been provided by the applicant. The applicant’s clinical overview has been written by an appropriately qualified person and is considered acceptable.

No new efficacy or safety studies have been performed and none are required for this type of application. A comprehensive review of the published literature has been provided by the applicant, citing the well-established clinical pharmacology, efficacy and safety of trazodone hydrochloride.

Based on the results of the bioequivalence studies, Trazodone Tablets can be considered bioequivalent to the reference products, Molipaxin 50mg/100mg Capsules and Molipaxin 150mg Tablets. (Winthrop Pharmaceuticals UK Limited).

IV.2 Pharmacokinetics
In support of these applications, the following bioequivalence studies were submitted:

STUDY 1
An open label, balanced, randomised, two-treatment, two-period, two-sequence, single dose, crossover, comparative oral bioavailability study of two formulations of Trazodone hydrochloride 150 mg Tablets (Accord Healthcare Limited) versus Molipaxin 150mg Tablets (Winthrop Pharmaceuticals UK Limited) in healthy, normal, adult, human subjects under fed conditions.
Following an overnight fast of at least 10 hours, subjects were served a high fat high calorific breakfast which they consumed completely within 30 minutes. Exactly after 30 minutes of the actual start time of the breakfast, subjects were administered a single dose of (1 x 150 mg Tablet) of the test of reference product. Blood samples were collected for plasma levels before dosing and up to and including 72 hours after the drug administration. The washout period between treatment phases was 10 days.

The main pharmacokinetic results are presented below:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Geometric Least Squares Mean Test Product-T</th>
<th>Geometric Least Squares Mean Reference Product-R</th>
<th>Ratio (T/R) %</th>
<th>90% Confidence Interval</th>
<th>Intra Subject CV (%)</th>
<th>Power (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>lnC&lt;sub&gt;max&lt;/sub&gt;</td>
<td>1926.623</td>
<td>2136.592</td>
<td>90.2</td>
<td>83.97 - 96.83</td>
<td>19.0</td>
<td>100.0</td>
</tr>
<tr>
<td>lnAUC&lt;sub&gt;0-t&lt;/sub&gt;</td>
<td>27928.880</td>
<td>27773.792</td>
<td>100.6</td>
<td>96.11 - 105.22</td>
<td>12.0</td>
<td>100.0</td>
</tr>
<tr>
<td>lnAUC&lt;sub&gt;0-∞&lt;/sub&gt;</td>
<td>29159.822</td>
<td>29631.416</td>
<td>98.4</td>
<td>94.69 - 102.27</td>
<td>10.2</td>
<td>100.0</td>
</tr>
</tbody>
</table>

The 90% confidence intervals of the test/reference ratio for AUC and C<sub>max</sub> values for trazodone lie within the acceptable limits of 80.00% to 125.00%, in line with the ‘Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr**). Thus, the data support the claim that the test product Trazodone Tablets (Accord Healthcare Limited) is bioequivalent to the reference product Molipaxin 150mg Tablets (Winthrop Pharmaceuticals UK Limited).

**STUDY 2**

An open label, balanced, randomised, two-treatment, two-period, two-sequence, single dose, crossover, comparative oral bioavailability study of two formulations of Trazodone hydrochloride 100 mg Tablets (Accord Healthcare Limited) versus Molipaxin 100 mg Capsules (Winthrop Pharmaceuticals UK Limited) in healthy, normal, adult, human subjects under fed conditions.

Following an overnight fast of at least 10 hours, subjects were served a high fat high calorific vegetarian breakfast which they consumed completely within 30 minutes. Exactly after 30 minutes of the actual start time of the breakfast, subjects were administered a single dose of (1 x 150 mg Tablet or 1 x 150 mg Capsule) of the test of reference product. Blood samples were collected for plasma levels before dosing and up to and including 72 hours after the drug administration. The washout period between treatment phases was 10 days.

The main pharmacokinetic results are presented below:
**Trazodone - pharmacokinetic parameters Study 2**
(non-transformed values; arithmetic mean ± SD, \( T_{\text{max}} \), median, range):

<table>
<thead>
<tr>
<th>Treatment</th>
<th>( \text{AUC}_{0-t} ) ( \text{ng/ml/h} )</th>
<th>( \text{AUC}_{0-\infty} ) ( \text{ng/ml/h} )</th>
<th>( C_{\text{max}} ) ( \text{ng/ml} )</th>
<th>( t_{\text{max}} ) h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>20337.835 ± 6630.1876</td>
<td>21495.465 ± 7596.5209</td>
<td>1166.095 ± 241.4450</td>
<td>3.000</td>
</tr>
<tr>
<td>Reference</td>
<td>19697.121 ± 7144.8302</td>
<td>20834.467 ± 8114.8549</td>
<td>1305.824 ± 505.3177</td>
<td>2.667</td>
</tr>
</tbody>
</table>

\[ \text{Ratio (90\% CI)} \] 106.1 (97.18-115.87) 106.1 (97.40-115.52) 94.7 (85.69-104.68)

AUC\(_{0-t}\) Area under the plasma concentration curve from administration to last observed concentration at time \( t \).

AUC\(_{0-\infty}\) Area under the plasma concentration curve extrapolated to infinite time.

\( C_{\text{max}} \) Maximum plasma concentration.

\( t_{\text{max}} \) Time until \( C_{\text{max}} \) is reached (Median (Min-Max)).

*Non-transformed values*

The 90% confidence intervals of the test/reference ratio for AUC and \( C_{\text{max}} \) values for trazodone lie within the acceptable limits of 80.00% to 125.00%, in line with the ‘Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr**). Thus, the data support the claim that the test product Trazodone Tablets (Accord Healthcare Limited) is bioequivalent to the reference product Molipaxin 100 mg Capsules (Winthrop Pharmaceuticals UK Limited).

**Biowaiver**

The justification for biowaiver for the 50 mg strength can be accepted as per EMA guideline on the investigation of bioequivalence (Doc. Ref.: CPMP/EWP/QWP/1401/98 Rev.1/Corr**; 20 January 2010) states if bioequivalence has been demonstrated at the strength(s) that are most sensitive to detect a potential difference between products, in vivo bioequivalence studies for the other strength(s) can be waived. As the 50 mg strength test product meets the biowaiver criteria specified in the current bioequivalence guidance, the results and conclusions of the bioequivalence study with the 100 mg and 150 mg tablet strength can be extrapolated to the 50 mg strength tablets.

**Conclusion**

Clinical studies have demonstrated bioequivalence of Trazodone Tablets (Accord Healthcare Limited) 150mg and 100mg to the corresponding reference products. Since biowaiver criteria are fulfilled, the conclusions from the bioequivalence studies can also be applied to the 50mg strength.

**IV.3 Pharmacodynamics**

No new pharmacodynamic data were submitted and none were required for applications of this type.

**IV.4 Clinical efficacy**

No new efficacy data were submitted and none were required for applications of this type.

**IV.5 Clinical safety**

With the exception of the safety data collected during the bioequivalence study, no new data on safety have been submitted and none are required for applications of this type. No new or unexpected adverse events were observed in the bioequivalence studies.

**IV.6 Risk Management Plan (RMP) and Pharmacovigilance System**

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended.
There are no differences from the reference product in terms of proposed uses, maximum pack size / strength or pharmaceutical form / formulation that would have any implications for safety.

In line with the reference product, the applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns (labelling in the SmPC and the PIL), which is acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

Periodic Safety Update Report (PSUR)

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorised under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

IV.7 Discussion on the clinical aspects
The grant of a marketing authorisation is recommended for this application from a clinical viewpoint.

V User consultation
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Solifenacin succinate 5/10mg film-coated tablets, (DK/H/2339/001-002/DC). The bridging report submitted by the applicant has been found acceptable.

VI Overall conclusion, benefit/risk assessment and recommendation
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with trazodone hydrochloride is considered to have demonstrated the therapeutic value of the compound. The results of the clinical study confirm that the product is bioequivalent to the reference product and its benefit-risk is, therefore, considered to be positive.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The MAH has submitted the following approved labelling for Trazodone Tablets which is presented below:
Trazodone hydrochloride
50 mg, 100 mg and 150 mg tablets

Trazodone hydrochloride tablets
Each tablet contains 50 mg trazodone hydrochloride.

84 x 1 tablets

Oral use.
Read the package leaflet before use.
Keep out of the sight and reach of children.

Take after food.
Store in the original package in order to protect from light.

Trazodone hydrochloride tablets
50 mg, 50 mg

UK/H/6352/001-003/DC
PAR Trazodone Hydrochloride 50 mg, 100 mg and 150 mg tablets

UK/H/6352/001-003/DC
Trazodone Hydrochloride 50 mg, 100 mg and 150 mg tablets

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Annex 1

Table of content of the PAR update
Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

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<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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