FLUOXETINE 20 MG/5 ML ORAL SOLUTION
(fluoxetine hydrochloride)

PL 36390/0001

UKPAR

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Fluoxetine 20 mg/5 ml Oral Solution

PL 36390/0001

LAY SUMMARY

The Medicine and Healthcare Regulatory Agency (MHRA) granted STD Chemicals Limited a Marketing Authorisation (licence) for the medicinal product Fluoxetine 20 mg/5 ml Oral Solution on 05 July 2012. This is a prescription only medicine (POM).

Fluoxetine belongs to a group of medicines called selective serotonin reuptake inhibitors (SSRIs). These work by bringing the level of serotonin in the brain, back up to normal. Low levels of serotonin are thought to be a cause of depression and related disorders.

Fluoxetine 20 mg/5ml Oral Solution is used to treat the following conditions in adults:

- Major depressive episodes
- Obsessive-compulsive disorder (OCD) an illness linked to anxiety in which you can become constantly troubled by persistent ideas (obsessions), that make you carry out repetitive rituals (compulsions)
- Bulimia nervosa (an eating disorder); fluoxetine is used alongside psychotherapy for the reduction of binge-eating and purging activity.

In children and adolescents aged 8 years and above, Fluoxetine 20 mg/5 ml Oral Solution is used to treat moderate to severe major depressive disorder, if the depression does not respond to psychological therapy after 4-6 sessions. Fluoxetine 20 mg/5 ml Oral Solution should be offered to a child or young person with moderate to severe depression only in combination with a psychological therapy.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Fluoxetine 20 mg/5 ml Oral Solution outweigh the risks, hence a Marketing Authorisation has been granted.
Fluoxetine 20 mg/5 ml Oral Solution

PL 36390/0001

SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted a Marketing Authorisation for the medicinal product Fluoxetine 20 mg/5 ml Oral Solution (PL 36390/0001) to STD Chemicals Limited on 05 July 2012. This is a prescription only medicine (POM).

Fluoxetine 20 mg/5ml Oral Solution is used to treat the following conditions in adults:

- Major depressive episodes
- Obsessive-compulsive disorder (OCD).
- Bulimia nervosa - Fluoxetine 20mg/5ml Oral Solution is indicated as a complement of psychotherapy for the reduction of binge-eating and purging activity.

In children and adolescents aged 8 years and above, Fluoxetine 20 mg/5 ml Oral Solution is used to treat moderate severe major depressive episode, if depression is unresponsive to psychological therapy after 4-6 sessions. Antidepressant medication should be offered to a child or young person with moderate to severe depression only in combination with a concurrent psychological therapy.

The application was submitted as a simple abridged application, according to Article 10c of Directive 2001/83/EC as amended, cross-referring to Fluoxetine 20mg/5ml Oral Solution (PL 20417/0045), which was originally granted a Marketing Authorisation (PL 08137/0088) to Neolab Limited on 27 February 2007. On 12 August 2011, the Marketing Authorisation Holder was updated by a change of ownership to Fannin (UK) Limited.

No new data was submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 36390/0001
PROPRIETARY NAME: Fluoxetine 20 mg/5 ml Oral Solution
ACTIVE(S): Fluoxetine hydrochloride
COMPANY NAME: STD Chemicals Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: POM

1. INTRODUCTION
This is an abridged simple, informed consent application for Fluoxetine 20 mg/5 ml Oral Solution submitted under Article 10c of Directive 2001/83/EC, as amended. The proposed Marketing Authorisation Holder is STD Chemicals Limited, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW, United Kingdom.

The application cross-refers to Fluoxetine 20mg/5ml Oral Solution (PL 20417/0045), which was originally granted a Marketing Authorisation (PL 08137/0088) to Neolab Limited on 27 February 2007. On 12 August 2011, the Marketing Authorisation Holder was updated by a change of ownership to Fannin (UK) Limited.

The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed name of the product is Fluoxetine 20 mg/5 ml Oral Solution. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product is for oral administration. Each 5 ml of oral solution contains 20 mg fluoxetine as the hydrochloride.

The medicine is packaged in amber Type III glass bottles with polypropylene lids, with low density polyethylene (LDPE) liners, containing 70 ml of oral solution, enclosed in outer cartons

The proposed shelf-life (24 months) and storage conditions (Store in the original package in order to protect from light) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a prescription only medicine (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
STD Chemicals Limited, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW, United Kingdom.

The qualified person 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 product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

European Directorate for the Quality of Medicines (EDQM) Certificates of Suitability for the drug substance manufacturers have been provided to support the manufacturing and control of the active substance. These details are in line with those of the reference product.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross reference product.

None of the excipients are sourced from genetically modified organisms.

2.11 Bioequivalence
No bioequivalence data are required to support this simple abridged application, as the proposed product is manufactured to the same formula utilising the same process as the cross-reference product Fluoxetine 20mg/5ml Oral Solution (PL 20417/0045).

3. EXPERT REPORTS
The applicant cross-refers to the data for Fluoxetine 20mg/5ml Oral Solution (PL 20417/0045), to which it claims identicality. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the cross-reference product.
6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
The patient information leaflet has been prepared in line with the details registered for the cross-reference product.

Neolab Limited have previously submitted results of PIL user testing, in accordance with Article 59 of Council Directive 2001/83/EC for the reference product Fluoxetine 20mg/5ml Oral Solution (PL 08137/0088). The results indicate that the 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.

As the leaflet for the reference product and this product is considered the same, no further user testing of the leaflet for this product is necessary. The Marketing Authorisation Holder has provided a report to bridge the leaflet for Fluoxetine 20 mg/5 ml Oral Solution; PL 36390/0001 (daughter) to the parent leaflet for the reference product (Fluoxetine 20mg/5ml Oral Solution (PL 08137/0088). This is acceptable as the PIL for PL 08137/0088 is the same as the current cross-reference product (PL 20417/0045).

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging.

7. CONCLUSIONS
The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

No new non-clinical data have been submitted with this application and none are required for an application of this type.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As the application is for an identical version of an already authorised reference product, it is not expected that the environmental exposure to fluoxetine hydrochloride will increase following the marketing approval of the product.

The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

No new clinical data have been submitted with this application and none are required for an application of this type.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the Marketing Authorisation Holder 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.

The Marketing Authorisation Holder has provided an adequate justification for not submitting a Risk Management Plan (RMP). As the application is for an identical version of an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference product has been in use for many years and the safety profile of the active ingredient is well-established.

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

QUALITY
The data for this application is consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

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

EFFICACY
This application is identical to a previously granted application for Fluoxetine 20mg/5ml Oral Solution (PL 20417/0045). No new or unexpected safety concerns arise from this application.

The SmPC, leaflet and labelling are satisfactory and consistent with that for the cross-reference product.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with fluoxetine hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
Fluoxetine 20 mg/5 ml Oral Solution

PL 36390/0001

STEPS TAKEN FOR ASSESSMENT

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<td>1</td>
<td>The MHRA received the marketing authorisation application on 22 December 2010.</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 07 February 2011.</td>
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<td>Following assessment of the application the MHRA requested further information on 09 March 2011, 16 November 2011 and 23 February 2012.</td>
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<td>The applicant responded to the MHRA’s request, providing further information on 05 September 2011, 13 February 2012 and 05 March 2012.</td>
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<td>The application was determined on 05 July 2012.</td>
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Fluoxetine 20 mg/5 ml Oral Solution

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STEPS TAKEN AFTER ASSESSMENT

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Fluoxetine 20 mg/5 ml Oral Solution

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SUMMARY OF PRODUCT CHARACTERISTICS

The Summary of Product Characteristics for this product is published on the MHRA website.
PRODUCT INFORMATION LEAFLET

The Patient Information Leaflet for this product is published on the MHRA website.