Fexofenadine Hydrochloride 120 mg Film-coated Tablets
Fexofenadine Hydrochloride 180 mg Film-coated Tablets

PL 36390/0053-4

UKPAR

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LAY SUMMARY

Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets
(Fexofenadine hydrochloride, film-coated tablets, 120 mg and 180 mg)

This is a summary of the Public Assessment Report (PAR) for Fexofenadine Hydrochloride 120 mg Film-coated Tablets (PL 36390/0053) and Fexofenadine Hydrochloride 180 mg Film-coated Tablets (PL 36390/0054). It explains how Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated 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 Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets.

For practical information about using Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets and what are they used for?
Fexofenadine Hydrochloride 120 mg Film-coated Tablets are used to relieve the symptoms of:
- hay fever (seasonal allergic rhinitis), such as sneezing, itchy and runny nose and red, itchy and watery eyes.

Fexofenadine Hydrochloride 180 mg Film-coated Tablets are used to relieve the symptoms of:
- long term allergic skin reactions (chronic idiopathic urticaria) such as itching, swelling and rashes.

Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets are not suitable for children under 12 years of age.

This medicine is identical to Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 08137/0121-2) which were first granted Marketing Authorisations to Neolab Limited on 25th March 2011.

How are Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets used?
The patient should always take this medicine exactly as the patient’s doctor has told them to. The patient should check with their doctor or pharmacist if they are not sure.

Dosage:
Adults and children 12 years and over
The recommended dose is one tablet (120 mg or 180 mg) daily. The patient should take the tablet with water before a meal.
Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets can be obtained only with a prescription.

For further information on how Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**How do Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets work?**
The active ingredient, fexofenadine hydrochloride, belongs to a group of medicines called non-sedating antihistamines which work by preventing the actions of histamine. Histamine is a substance produced by the body as part of its defence mechanisms. It is stored in cells called mast cells, in almost all tissues of the body. When the body reacts to a foreign substance (known as an allergen, e.g. flower pollen), the mast cells stimulated by the allergen release their stores of histamine. The released histamine then binds to its receptors (called H1 receptors) causing a chain reaction that results in allergic symptoms. This medicine works by blocking histamine H1 receptors and therefore stops the chain reaction that results in allergic symptoms.

**What benefits of Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets have been shown in studies?**
The applications for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets are considered to be identical to the previously authorised applications for Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 08137/0121-2), with the same benefits and risks. So, no new studies have been provided for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets. However, reference is made to the studies for Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 08137/0121-2).

The company (STD Chemicals Limited) referred to data provided by Neolab Limited for the grant of the licences for Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 08137/0121-2) as a basis for the grant of identical licences for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 36390/0053-0054).

**What are the possible side effects from Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 36390/0053-0054) are considered to be identical to the previously authorised applications for Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 08137/0121-2) with the same benefits and risks.

For a full list of all the side effects reported with Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.
Why are Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets approved?
No new or unexpected safety concerns arose from these applications. The MHRA, therefore, considered that the benefits of Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets outweigh their risks; and the grant of Marketing Authorisations (licences) was recommended.

What measures are being taken to ensure the safe and effective use of Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets?
Safety information has been included in the Summaries of Product Characteristics and the package leaflet for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated 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 Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets
Marketing Authorisations were granted in the UK on 19th September 2011.

The full PAR for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets follows this summary.

For more information about treatment with Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in June 2015
Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets

PL 36390/0053-4

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted STD Chemicals Limited Marketing Authorisations for the medicinal products Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 36390/0053-4) on 19th September 2011. The products are prescription-only medicines.

These are simple, abridged, ‘informed consent’ applications, submitted according to Article 10(c) of EC Directive 2001/83 (as amended), cross-referencing the Marketing Authorisations for Fexofenadine Hydrochloride 120 mg and 180 mg Film-coated Tablets (PL 08137/0121-2), authorised to Neolab Limited on 25th March 2011 through incoming Mutual Recognition procedures [IE/H/0230/001-2/MR] where Ireland was the Reference Member State (RMS).

Fexofenadine Hydrochloride 120 mg Film-coated Tablets are indicated in adults and children aged 12 years and over for the relief of symptoms associated with seasonal allergic rhinitis.

Fexofenadine Hydrochloride 180 mg Film-coated Tablets are indicated in adults and children aged 12 years and over for the relief of symptoms associated with chronic idiopathic urticaria.

Fexofenadine hydrochloride is a non-sedating H₁ antihistamine (ATC code: RO6AX26). It is a pharmacologically active metabolite of terfenadine. Human histamine wheal and flare studies following single and twice daily doses of fexofenadine hydrochloride demonstrate that the drug exhibits an antihistaminic effect beginning within one hour, achieving maximum at 6 hours and lasting 24 hours. There is no evidence of tolerance to these effects after 28 days of dosing. A positive dose-response relationship between doses of 10mg to 130mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130mg were required to achieve a consistent effect that was maintained over a 24 hour period. Maximum inhibition in skin wheal and flare areas was greater than 80%. Clinical studies conducted in seasonal allergic rhinitis have shown that a dose of 120mg is sufficient for 24 hour efficacy.

The MHRA considers that the pharmacovigilance system described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the services of a Qualified Person (QP) 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 MAH has provided adequate justification for not submitting a Risk Management Plan (RMP). As the applications are for products that are identical to already authorised reference products, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference products have been in use for many years and the safety profile of the active is well-established.
The MAH has provided adequate justification for not submitting an Environmental Risk Assessment (ERA). It is not considered that these medicinal products represent any risk to the environment. There is no reason to conclude that marketing of these products will change the overall use pattern of the existing market. The availability of these medicinal products, which are identical to the cited reference products, will not lead to any increase in environmental exposure concentrations of the active ingredient.

No new data were submitted nor was it necessary for these simple applications, as the data are identical to those of the previously granted cross-reference products.
II QUALITY ASPECTS

II.1. INTRODUCTION

These are simple abridged applications, submitted under Article 10(c) of Directive 2001/83/EC (as amended) for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets. The proposed MAH is STD Chemicals Ltd.

The reference products are Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 08137/0121-2) authorised to Neolab Limited on 25th March 2011 through incoming Mutual Recognition procedures [IE/H/0230/001-2/MR] where Ireland was the Reference Member State (RMS). The proposed and reference products are considered identical.

II.2. Drug Substance

Drug substance specification

The proposed drug substance specifications are consistent with the details registered for the cross-reference product.

II.3. Medicinal Product

Name(s)

The approved names of the products are Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets. The products have been named in line with current requirements and the product names are acceptable.

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

Each film-coated tablet contains 120 mg or 180 mg of the active ingredient fexofenadine hydrochloride, equivalent to 112 mg and 168 mg of fexofenadine respectively. The tablets are licensed for marketing in polyvinylchloride (PVC) / polyvinylidene chloride (PVdC) / aluminium foil blister strips, which are packed with the Patient Information Leaflet (PIL) into cardboard outer cartons, in pack sizes of 7, 10, 15, 20, 30, 50, 100 or 500 film-coated tablets. The MAH has stated that not all pack sizes may be marketed. The container closure systems and pack sizes are identical to those for the reference products.

The approved shelf-life (3 years) and storage conditions (‘Store the tablets in the original package. This medicinal product does not require any special temperature storage conditions’) are identical to the details registered for the reference products.

Legal status

POM - The products are available subject to a medical prescription.

Marketing Authorisation Holder / Contact Persons/Company

The proposed Marketing Authorisation Holder is ‘STD Chemicals Ltd, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW’.

The Qualified Person (QP) responsible for pharmacovigilance was stated and their CV included.
Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of GMP compliance has been provided.

Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the cross-reference products.

Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.

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 specifications are in line with the details registered for the cross-reference products.

TSE Compliance
The only excipient used that contains material of animal or human origin is magnesium stearate. Satisfactory documentation has been provided by the magnesium stearate supplier stating that the magnesium stearate they provide complies with the criteria described in the current version of the monograph ‘Products with risk of transmitting agents of animal spongiform encephalopathies’. None of the excipients are sourced from genetically modified organisms.

EXPERT REPORT
A satisfactory quality overall summary has been prepared by an appropriately qualified expert. The CV of the expert was provided.

PRODUCT NAME & APPEARANCE
See Section II.3 for details of the proposed product names. The 120 mg strength tablets are peach-coloured, oblong, biconvex, film coated tablets. The 180 mg strength tablets are yellow-coloured, oblong, biconvex, film coated tablets, plain on one side and with a central breakline on the reverse side. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses. The appearance of the products is identical to that of the cross-reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The approved SmPCs are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) / LABELLING
PIL
The approved PIL is satisfactory and in line with the approved SmPCs. It has been prepared according to the Quality Review of Documents (QRD) template and is consistent with the details registered for the cross-reference products.

Labelling
Mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference products and complies with statutory requirements.

The MAH has stated that not all licensed pack sizes may be marketed. They have committed to submitting mock-ups for currently unmarketed pack sizes to the MHRA for approval before those packs are commercially marketed.

7. CONCLUSIONS
The grounds for these applications are considered adequate. Marketing Authorisations were therefore granted.
III NON-CLINICAL ASPECTS

Introduction
These are simple, abridged, ‘informed consent’ applications made under Article 10(c) of EC Directive 2001/83 (as amended).

No new non-clinical data have been supplied with these applications and none are required for applications of this type. A non-clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the non-clinical expert has been supplied.

Ecotoxicity/environmental risk assessment (ERA)
The Marketing Authorisation Holder has provided adequate justification for not submitting an Environmental Risk Assessment (ERA).

Discussion on the non-clinical aspects
The grant of Marketing Authorisations is recommended.
IV  CLINICAL ASPECTS

These are simple, abridged, ‘informed consent’ applications made under Article 10(c) of EC Directive 2001/83 (as amended), cross-referring to the Marketing Authorisations for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 08137/0121-2; Neolab Limited).

No new clinical data have been supplied with the applications, and none are required for applications of this type. A clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the clinical expert has been supplied.

V  User consultation

PIL user-testing has been accepted based on bridging to the successful user-testing of the PIL for the reference products, Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 08137/0121-2). The text, content and layout of the proposed PIL are essentially identical to the approved PIL for the reference products. The bridging is accepted.
VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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

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

EFFICACY
These applications are considered identical to the previously granted licences for Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 08137/0121-2; Neolab Limited).

No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE
The approved SmPCs, PIL and labelling are satisfactory and consistent with the details registered for the cross-reference products.

PIL user-testing has been accepted based on bridging to the successful user-testing of the PIL for the reference products, Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets (PL 08137/0121-2).

The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging and sufficient space has been included for a standard UK pharmacy dispensing label. The MAH has stated that not all licensed pack sizes may be marketed. They have committed to submitting mock-ups for unmarketed pack sizes to the MHRA for approval before those packs are marketed.

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 cross-reference products. The benefit: risk ratio is considered to be positive.
Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets

PL 36390/0053-4

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the marketing authorisation applications on 5\textsuperscript{th} May 2011.

2. Following standard checks and communication with the applicant, the MHRA considered the applications valid on 3\textsuperscript{rd} June 2011.

3. Following assessment of the application, the MHRA requested further information relating to the quality dossier on 2\textsuperscript{nd} August 2011.

4. The applicant responded to the MHRA’s requests, providing further information for the quality sections on 15\textsuperscript{th} August 2011.

5. The applications were determined on 19\textsuperscript{th} September 2011.
Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets

PL 36390/0053-4

STEPS TAKEN AFTER AUTHORISATION

The following table lists non-safety updates to the Marketing Authorisations (PL 36390/0053-0054) for these products that have been approved by the MHRA since the products were first licensed. The table includes updates that have been added as an annex to this PAR. This is not a complete list of the post-authorisation changes that have been made to these Marketing Authorisations.

<table>
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<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>For PL 36390/0053 &amp; 0054; variation number 14 30 January 2015</td>
<td>Type 1B</td>
<td>To update SmPC sections 1, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1 and 5.2 in line with the reference product, Telfast 120mg film-coated tablets. Consequently the PIL, carton and blister mock-ups have been updated.</td>
<td>Approved 12 May 2015</td>
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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.
Product Information Leaflets
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.
Fexofenadine Hydrochloride 120 mg Film-coated Tablets

Carton for blisters
Braille

F E X O F E N A D I N E
H Y D R O C H L O R I D E
120 mg
#120 mg
F I L M - C O A T E D
T A B L E T S
Fexofenadine Hydrochloride 180 mg Film-coated Tablets

Carton for blisters

Fexofenadine Hydrochloride

180 mg Film-coated Tablets

Each tablet contains 180 mg of fexofenadine hydrochloride equivalent to 180 mg fexofenadine.

For oral administration. Use as directed by a physician.

Please read the enclosed leaflet.

Store the tablets in the original packaging.

This medicinal product does not require any special temperature storage conditions.

KEEP ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN

Fexofenadine Hydrochloride

180 mg Film-coated Tablets

Fexofenadine hydrochloride

30 Film-coated Tablets

Distributor:
Neodal Ltd., 57 High Street, Oxshott, Surrey, KT19 9LF.

PL 36390/0054

MA Holder: STD Chemicals Ltd, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW.
UKPAR Fexofenadine Hydrochloride 120 mg & 180 mg Film-coated Tablets

Braille

FEXOFENADINE HYDROCHLORIDE

#180 mg

Film-coated Tablets
ANNEX 1

Our Reference: PL 36390/0053-0014
               PL 36390/0054-0014

Product: Fexofenadine Hydrochloride 120 mg Film-coated Tablets
         Fexofenadine Hydrochloride 180 mg Film-coated Tablets

Marketing Authorisation Holder: Cipla (EU) Limited
Active Ingredient(s): Fexofenadine hydrochloride.

Type of Procedure: National
Submission Type: Variation
Submission Category: Type IB
Submission Complexity: Standard
EU Procedure Number (if applicable): Not applicable

Reason:
To update section 1, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1 and 5.2 of the Summary of Product Characteristics (SmPC) in line with the reference product, Telfast 120mg and 180 mg film-coated tablets. As a consequence, the Patient Information Leaflet (PIL), carton and blister mock-ups have been updated.

Supporting Evidence
Revised SmPC fragments, PIL and labelling.

Evaluation
The proposed changes to the SmPCs, and PIL are in line with the reference product. The updated SmPC fragments, PIL and labelling have been incorporated into the Marketing Authorisations:
Fexofenadine Hydrochloride 180 mg Film-coated Tablets

For oral use

MA Holder:
Cipla UK Limited,
Hillbro House, Hillbro Road, Esher,
Surrey, KT10 9WW, United Kingdom
PL 86391/005-4

FEXOFENADINE HYDROCHLORIDE 180 mg FILM-COATED TABLETS
Conclusion
The proposed changes to the SmPCs, PIL and labelling are acceptable.

Decision - Approved on 12 May 2015.