Public Assessment Report

Decentralised Procedure

Ezetimibe 10 mg Tablets

(Ezetimibe)

Procedure No: UK/H/6322/001/DC

UK Licence No: PL 35507/0180

Lupin (Europe) Limited
LAY SUMMARY

Ezetimibe 10 mg Tablets
(Ezetimibe)

This is a summary of the Public Assessment Report (PAR) for Ezetimibe 10 mg Tablets (PL 35507/0180; UK/H/6322/001/DC). It explains how the application for Ezetimibe 10 mg Tablets was assessed and its authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Ezetimibe 10 mg Tablets. The product may be referred to as ‘Ezetimibe’ in this Lay summary.

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

What is Ezetimibe and what is it used for?
Ezetimibe is a ‘generic’ medicine. This means that Ezetimibe is similar to a ‘reference’ medicine already authorised in the European Union (EU) called Ezetrol 10 mg Tablets (PL 00025/0609; Merck, Sharp & Dohme Limited, UK).

Ezetimibe is a medicine to lower increased levels cholesterol. Cholesterol is one of several fatty substances found in the bloodstream. The total cholesterol is made up mainly of LDL and HDL cholesterol. Ezetimibe lowers levels of total cholesterol, "bad" cholesterol (LDL cholesterol), and fatty substances called triglycerides in the blood. In addition, this medicine raises levels of "good" cholesterol (HDL cholesterol).

LDL cholesterol is often called “bad” cholesterol because it can build up in the walls of the arteries forming plaque. Eventually this plaque build-up can lead to a narrowing of the arteries. This narrowing can slow or block blood flow to vital organs such as the heart and brain. This blocking of blood flow can result in a heart attack or stroke.

HDL cholesterol is often called “good” cholesterol because it helps keep the bad cholesterol from building up in the arteries and protects against heart disease.

Triglycerides are another form of fat in the blood that may increase the risk for heart disease.

Ezetimibe is used for patients who cannot control their cholesterol levels by cholesterol lowering diet alone. The patient should stay on a cholesterol lowering diet while taking this medicine.

Ezetimibe is used in addition to a cholesterol lowering diet if the patient has:
- a raised cholesterol level in the blood (primary hypercholesterolaemia [heterozygous familial and non-familial])
  - together with a statin, when the patient’s cholesterol level is not well controlled with a statin alone
  - alone, when statin treatment is inappropriate or is not tolerated
- a hereditary illness (homozygous familial hypercholesterolaemia) that increases the cholesterol level in the blood. The patient will also be prescribed a statin and may also receive other treatments

If the patient suffers from heart disease, ezetimibe combined with cholesterol-lowering medicines called statins reduces the risk of heart attack, stroke, surgery to increase heart blood flow, or hospitalisation for chest pain.
Ezetimibe 10 mg Tablets

Ezetimibe does not help a patient to lose weight.

**How does Ezetimibe work?**
This medicine contains the active substance ezetimibe, which works by reducing the cholesterol absorbed in the digestive tract. Ezetimibe adds to the cholesterol-lowering effect of statins, a group of medicines that reduce the cholesterol the body makes by itself.

**How is Ezetimibe used?**
Ezetimibe is available as tablets and is taken by mouth (orally).

Ezetimibe can only be obtained with a prescription. The tablets should be taken exactly as told by the doctor or pharmacist. The patient should check with the doctor or pharmacist if not sure.

- Before starting Ezetimibe, the patient should be on a diet to lower his/her cholesterol.
- The patient should keep on this cholesterol lowering diet whilst taking Ezetimibe.

The recommended dose is one 10 mg tablet by mouth once a day. Ezetimibe can be taken any time of day, with or without food.

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

**What benefits of Ezetimibe has been shown in studies?**
As Ezetimibe is a generic medicine, studies have been limited to tests to determine that Ezetimibe is bioequivalent to the reference medicine Ezetrol (Merck, Sharp & Dohme Limited, UK). Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

**What are the possible side effects of Ezetimibe?**
Because Ezetimibe is a generic medicine and bioequivalent to the reference medicine Ezetrol 10 mg Tablets (Merck, Sharp & Dohme Limited, UK), the possible side effects are taken as being the same as those of the reference medicine.

For the full list of all side effects reported with Ezetimibe, see section 4 of the package leaflet.

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

**Why is Ezetimibe approved?**
It was concluded that, in accordance with EU requirements, Ezetimibe has been shown to have comparable quality and to be bioequivalent to Ezetrol 10 mg Tablets (Merck, Sharp & Dohme Limited, UK). Therefore, the view was that, as for Ezetrol (Merck, Sharp & Dohme Limited, UK), the benefits outweigh the identified risks.

**What measures are being taken to ensure the safe and effective use of Ezetimibe?**
A Risk Management Plan has been developed to ensure that Ezetimibe is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics (SmPC) and the package leaflet for Ezetimibe, 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 and healthcare professionals will be monitored and reviewed continuously as well.
Other information about Ezetimibe

Hungary and the UK agreed to grant a Marketing Authorisation for Ezetimibe on 04 May 2017. A Marketing Authorisation was granted in the UK to Lupin (Europe) Limited on 31 May 2017.

The full PAR for Ezetimibe follows this summary.

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

This summary was last updated in July 2017.
SCIENTIFIC DISCUSSION

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Scientific Discussion

I INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the UK and Hungary considered that the application for Ezetimibe 10 mg Tablets (PL 35507/0180; UK/H/6322/001/DC) could be approved. The product may be referred to as ‘Ezetimibe’ in this Scientific discussion.

Ezetimibe is a Prescription Only Medicine (POM) and is indicated in the following:

• **Primary Hypercholesterolaemia**
  Ezetimibe co-administered with an HMG-CoA reductase inhibitor (statin) is indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolaemia who are not appropriately controlled with a statin alone.

  Ezetimibe monotherapy is indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolaemia in whom a statin is considered inappropriate or is not tolerated.

• **Prevention of Cardiovascular Events**
  Ezetimibe is indicated to reduce the risk of cardiovascular events (see section 5.1 of the SmPC) in patients with coronary heart disease (CHD) and a history of acute coronary syndrome (ACS) when added to ongoing statin therapy or initiated concomitantly with a statin.

• **Homozygous Familial Hypercholesterolaemia (HoFH)**
  Ezetimibe, co-administered with a statin, is indicated as adjunctive therapy to diet for use in patients with HoFH. Patients may also receive adjunctive treatments (e.g. LDL apheresis).

This application was submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS) and Hungary as Concerned Member State (CMS). The application was submitted under Article 10(1) of Directive 2001/83/EC, as amended, claiming to be a generic medicinal product of the originator medicinal product Ezetrol 10 mg Tablets (PL 00025/0609; Merck, Sharp & Dohme Limited, UK), which was first authorised in the UK on 03 April 2002 following an in-coming Decentralised Procedure (DE/H/0396/001) with Germany as RMS and the UK as a CMS.

The active substance ezetimibe, is a selective inhibitor of intestinal absorption for cholesterol and related plant sterols, via the NPC1L1 sterol transporter.

One bioequivalence study, comparing the applicant’s test product Ezetimibe 10 mg tablets with the reference product Ezetrol 10 mg Tablets (Merck, Sharp & Dohme Limited, UK) under fasting condition, was submitted to support the application. It is stated that the bioequivalence study was conducted in accordance with Good Clinical Practice (GCP) and the Declaration of Helsinki.

With the exception of the bioequivalence study, no new non-clinical or clinical studies were conducted, which is acceptable given that the subject of this application is a generic medicinal product of an originator product that have been licensed for over 10 years.

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place at all sites responsible for the manufacture, assembly and batch release of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturing authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.
For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, ‘close-out letters’ or ‘exchange of information’ issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

The UK and Hungary considered that the application could be approved at the end of procedure (Day 210) on 04 May 2017. After a subsequent national phase, a Marketing Authorisation was granted in the UK to Lupin (Europe) Limited on 31 May 2017.

II QUALITY ASPECTS
II.1 Introduction
The submitted documentation concerning the proposed product is of sufficient quality and meets the current EU regulatory requirements.

The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Ezetimibe 10 mg Tablets are white to off-white, capsule shaped, flat-faced, bevelled-edge tablets, 8.1 mm x 4 mm and debossed with “E” on one side and “10” on the other side.

Each tablet contains 10 mg ezetimibe, as the active substance.

The product also contains pharmaceutical excipients, namely lactose monohydrate, Povidone (K-30), sodium lauryl sulfate, crospovidone, anhydrous silica colloidal and stearic acid. Appropriate justification for the inclusion of each excipient has been provided.

The finished product is supplied in:
1. polyvinylchloride/Aclar or aluminium blisters with aluminium lidding foil containing 1,20, 28, 30, 50, 90,98 or 100 tablets
2. aluminium/oriented polyamide/high density polyethylene-desiccant coated blisters with aluminium lidding foil containing 1, 20, 28, 30, 50, 90, 98 or 100 tablets
3. high density polyethylene bottles with child-resistant closures containing either an oxygen absorbing sachet or desiccant sachet containing 30 tablets.

Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis for the primary packaging materials have been provided. All primary packaging complies with current European regulations concerning materials in contact with foodstuff.

II.2 DRUG SUBSTANCE
Ezetimibe
INN: Ezetimibe
Chemical name: (3R, 4S)-1- (4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-2-azetidinone
1-(4-fluorophenyl)-3(R)-[3-(4-fluorophenyl)-3(S)-hydroxypropyl]-4(S)-(4-hydroxyphenyl)-2-azetidinone
Molecular formula: C_{24}H_{21}F_{2}NO_{3}

M_r: 409.43

Appearance: White to off-white crystalline powder.

Solubility: Free soluble in methanol and in acetone, soluble in ethanol, practically insoluble in water.

Ezetimibe was not the subject of a European Pharmacopoeia monograph at the time of assessment.

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 formulate safe, efficacious, stable tablets, each containing 10 mg of ezetimibe which were bioequivalent to Ezetrol 10 mg Tablets (Merck, Sharp & Dohme Limited, UK). Suitable pharmaceutical development data have been provided for this application.

Comparative in-vitro dissolution profiles have been provided for this product and the reference product. The dissolution profiles were satisfactory.

All excipients comply with their respective European Pharmacopoeia monographs.

With the exception of lactose monohydrate, none of the excipients contain materials of animal or human origin. The supplier of lactose monohydrate has confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the supplier has confirmed that no ruminant material, other than calf rennet, is used during the production of lactose monohydrate.
No genetically modified organisms (GMO) have been used in the preparation of these excipients.

**Manufacturing Process**
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate description of the manufacturing process. The manufacturing process has been validated with full-scale production batches and has shown satisfactory results.

**Control of Finished Product**
The finished product specification is acceptable. Test methods have been described and have been validated adequately. Batch data have been provided that comply with the release specification. 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 finished product in the packaging proposed for marketing. Based on the results, a shelf-life of 2 years, with special storage instructions of ‘Store below 25°C,’ has been accepted.

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

**Bioequivalence/Bioavailability**
Satisfactory Certificates of Analysis have been provided for the test and reference batches used in the bioequivalence study. The bioequivalence study is discussed in Section IV, Clinical Aspects.

**II.4 Discussion on chemical, pharmaceutical and biological aspects**
It is recommended that a Marketing Authorisation is granted for this application, from a quality point of view.

**III NON-CLINICAL ASPECTS**

**III.1 Introduction**
The pharmacodynamic, pharmacokinetic and toxicological properties of ezetimibe are well known. No new non-clinical data have been submitted for this application and none are required given the clinical data study and the pharmaceutical comparative data that have been submitted.

The applicant has provided an overview based on published literature. The non-clinical overview 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**
No new data have been submitted and none are required for an application of this type. Refer to Section III.1, Introduction, above.

**III.3 Pharmacokinetics**
No new data have been submitted and none are required for an application of this type. Refer to Section III.1, Introduction, above.

**III.4 Toxicology**
No new data have been submitted and none are required for an application of this type. Refer to Section III.1, Introduction, above.
III.5 Ecotoxicity/Environmental Risk Assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is for a generic version of already authorised product, it is not expected that environmental exposure of ezetimibe will increase following approval of the Marketing Authorisation for the proposed product. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

III.6 Discussion of the non-clinical aspects
It is recommended that a Marketing Authorisation is granted, from a non-clinical point of view.

IV. CLINICAL ASPECTS
IV.1 Introduction.
The clinical pharmacology of ezetimibe is well-known.

With the exception of data from the bioequivalence study detailed in Section IV.2, Pharmacokinetics below, no new pharmacokinetic data is provided or required for this application. In line with the bioequivalence guideline, the results for free (unconjugated) ezetimibe are the key analysis for the bioequivalence estimation.

IV.2 Pharmacokinetics
The clinical pharmacology of ezetimibe is well-known. Ezetimibe is metabolised primarily in the small intestine and liver via glucuronide conjugation with subsequent biliary excretion. Ezetimibe and ezetimibe-glucuronide are the major drug-derived compounds detected in plasma, constituting approximately 10 to 20 % and 80 to 90 % of the total drug in plasma, respectively.

In support of the application, the applicant submitted the following bioequivalence study:

An open-label, randomised, two-treatment, two-sequence, two-period, single-dose, crossover, bioequivalence study comparing the test product Ezetimibe 10 mg tablets versus the reference product Ezetrol 10 mg tablets (MSD, UK) in healthy adult subjects under fasting conditions.

Subjects were administered a single oral dose of either the test or reference product with 240 ml of water after an overnight fast. Blood sampling was performed pre-dose and up to 72 hours post dose in each treatment period. A washout period of 11 days was kept between each consecutive dosing period. The pharmacokinetic results are presented below for unconjugated ezetimibe.

<table>
<thead>
<tr>
<th>PK Parameter</th>
<th>N</th>
<th>Geometric Least Square Means</th>
<th>T/R Ratio (%)</th>
<th>90% Confidence Interval</th>
<th>ISCV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Test (T)</td>
<td>Reference (R)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_{max}</td>
<td>43</td>
<td>4504.2593</td>
<td>4280.1449</td>
<td>105.24</td>
<td>95.95</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>115.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>25.45</td>
</tr>
<tr>
<td>AUC_{0-t}</td>
<td>43</td>
<td>80935.5699</td>
<td>82986.8996</td>
<td>97.53</td>
<td>90.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>105.30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21.11</td>
</tr>
</tbody>
</table>

AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours

C_{max} maximum plasma concentration

ISCV intra-subject coefficient of variation

Bioequivalence Discussion and Conclusion
The Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr*) defines the confidence limits for ratio of geometric means for acceptance of bioequivalence as 80.00% to 125.00% for C_{max} and AUC values. The results indicate that the bioequivalence criteria are met for unconjugated ezetimibe as the AUC_{0-t} and C_{max} values lie within acceptance limits. Hence, the data from this study support the claim that the applicant’s test product is bioequivalent to the reference.
product, Ezetrol 10 mg Tablets (Merck, Sharp & Dohme Limited, UK), under fasting conditions.

IV.3 Pharmacodynamics
The clinical pharmacodynamics properties of ezetimibe are well-known. No new pharmacodynamic data were submitted and none are required for an application of this type.

IV.4 Clinical Efficacy
The clinical efficacy of ezetimibe is well-known. No new efficacy data are presented or are required for an application of this type.

IV.5 Clinical Safety
No new safety data were submitted and none are required for an application of this type. No new or unexpected safety issues arose during the bioequivalence study.

IV.6 Risk Management Plan
The MAH has submitted a Risk Management Plan (RMP), in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Ezetimibe.

A summary of safety concerns is listed in the table below:

<table>
<thead>
<tr>
<th>Safety Concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important identified risk(s)</td>
</tr>
<tr>
<td>1. Rhabdomyolysis/myopathy</td>
</tr>
<tr>
<td>2. Abnormal liver function</td>
</tr>
<tr>
<td>3. Hypersensitivity</td>
</tr>
<tr>
<td>4. Drug interaction with ciclosporin</td>
</tr>
<tr>
<td>5. Drug interaction with warfarin, another coumarin anticoagulant, or fluindione</td>
</tr>
<tr>
<td>Important potential risk(s)</td>
</tr>
<tr>
<td>1. Cholecystitis/cholelithiasis</td>
</tr>
<tr>
<td>2. Pancreatitis</td>
</tr>
<tr>
<td>Missing information</td>
</tr>
<tr>
<td>1. Use during pregnancy</td>
</tr>
<tr>
<td>2. Use during lactation</td>
</tr>
<tr>
<td>3. Limited exposure in children age 10 to 17 beyond 1 year and limited exposure in children less than 10 years of age</td>
</tr>
</tbody>
</table>

Routine pharmacovigilance and risk minimisation activities are planned for all safety concerns which are considered acceptable.

IV.7 Discussion of the clinical aspects
It is recommended that a Marketing Authorisation is granted, from a clinical point of view.

V. USER CONSULTATION
A package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended. The language used for the purpose of user testing the package information leaflet (PIL) was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.
VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY
The important quality characteristics of Ezetimibe are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type. As the pharmacokinetics, pharmacodynamics and toxicology of ezetimibe are well-known, no additional data were required.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s test product and the reference product Ezetrol 10 mg Tablets (Merck, Sharp & Dohme Limited, UK), under fasting conditions.

SAFETY
No new data were submitted and none are required for an application of this type. As the safety profile of ezetimibe is well-known, no additional data were required. No new or unexpected safety concerns arose from the safety data from the bioequivalence study.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory and in line with current guidance.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with ezetimibe is considered to have demonstrated the therapeutic value of the compound. The product is bioequivalent to the marketed reference product. The overall benefit/risk assessment is therefore considered to be positive.

RECOMMENDATION
The grant of a Marketing Authorisation is recommended.
In accordance with Directive 2010/84/EU, the current version of the SmPC and PIL are available on the MHRA website. The current labelling is presented below:

The labelling text below is that agreed at the end of the Decentralised procedure. The Marketing Authorisation Holder has committed to submit the labelling for review to the regulatory authorities before marketing any pack size.

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING**

**CARTON AND BOTTLE LABEL**

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ezetimibe 10 mg Tablets</td>
</tr>
<tr>
<td>Ezetimibe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. STATEMENT OF ACTIVE SUBSTANCE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each tablet contains 10 mg ezetimibe.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. LIST OF EXCIPIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contains lactose monohydrate. See leaflet for further information.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. PHARMACEUTICAL FORM AND CONTENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets</td>
</tr>
<tr>
<td>1 Tablets</td>
</tr>
<tr>
<td>20 Tablets</td>
</tr>
<tr>
<td>28 Tablets</td>
</tr>
<tr>
<td>30 Tablets</td>
</tr>
<tr>
<td>50 Tablets</td>
</tr>
<tr>
<td>90 Tablets</td>
</tr>
<tr>
<td>98 Tablets</td>
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<tr>
<td>100 Tablets</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>5. METHOD AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read the package leaflet before use.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keep out of the sight and reach of children.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. OTHER SPECIAL WARNING(S), IF NECESSARY</th>
</tr>
</thead>
</table>
8. **EXPIRY DATE**

EXP:

9. **SPECIAL STORAGE CONDITIONS**

Store below 25°C.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Lupin (Europe) Limited  
Victoria Court, Bexton Road,  
Knutsford, Cheshire,  
WA16 0PF  
United Kingdom

12. **MARKETING AUTHORISATION NUMBER(S)**

PL 35507/0180

13. **BATCH NUMBER**

Lot:

14. **GENERAL CLASSIFICATION FOR SUPPLY**

POM

15. **INSTRUCTIONS ON USE**

16. **INFORMATION IN BRAILLE**

Ezetimibe 10 mg Tablets
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLISTER STRIPS</td>
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</table>

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT</th>
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<tbody>
<tr>
<td>Ezetimibe 10 mg Tablets</td>
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<tr>
<td>Ezetimibe</td>
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<table>
<thead>
<tr>
<th>2. NAME OF THE MARKETING AUTHORISATION HOLDER</th>
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<tbody>
<tr>
<td>Lupin (Europe) Limited</td>
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<table>
<thead>
<tr>
<th>3. EXPIRY DATE</th>
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<tbody>
<tr>
<td>EXP:</td>
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<table>
<thead>
<tr>
<th>4. BATCH NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lot:</td>
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<table>
<thead>
<tr>
<th>5. OTHER</th>
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</thead>
</table>
Annex 1 - Table of content of the PAR update for MRP and DCP

Steps Taken After The Initial Procedure With An Influence On The Public Assessment Report

<table>
<thead>
<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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