Public Assessment Report

Decentralised Procedure

Ezetimibe 10 mg Tablets (ezetimibe)

UK/H/6438/001/DC

UK licence no: PL 34424/0005

Key Pharmaceuticals Ltd.
LAY SUMMARY

Ezetimibe 10 mg Tablets
(ezetimibe)

This is a summary of the Public Assessment Report (PAR) for Ezetimibe 10 mg Tablets (PL 34424/0005; UK/H/6438/001/DC). It explains how Ezetimibe 10 mg Tablets was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

For practical information about using Ezetimibe 10 mg Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Ezetimibe 10 mg Tablets and what are they used for?
Ezetimibe 10 mg Tablets is a ‘generic medicine’. This means that Ezetimibe 10 mg Tablets is similar to a ‘reference medicine’ already authorised in the European Union (EU) called Ezetrol 10mg Tablets.

Ezetimibe tablets are used by patients who cannot control their cholesterol levels by cholesterol lowering diet alone. The patient should stay on their cholesterol lowering diet while taking Ezetimibe tablets. Cholesterol is one of several fatty substances found in the bloodstream. Total cholesterol is made up mainly of LDL and HDL cholesterol. Ezetimibe tablets lowers levels of “bad” cholesterol (LDL cholesterol), and fatty substances called triglycerides in the blood. In addition, Ezetimibe tablets increases levels of “good” cholesterol (HDL cholesterol) in the blood.

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. It is used for patients who cannot control their cholesterol levels by cholesterol lowering diet alone. Tablets are used in addition to the patient’s cholesterol lowering diet if the patient has:

- a raised cholesterol level in your blood [primary hypercholesterolaemia (heterozygous familial and non-familial)]
  - together with a statin, when your cholesterol level is not well controlled with a statin alone
  - alone, when statin treatment is unsuitable or is not tolerated
- a hereditary illness that increases the cholesterol level in the blood (homozygous familial hypercholesterolaemia). The patient will also be prescribed a statin and may also receive other treatments
- a hereditary illness that increases the levels of plant sterols in the blood (homozygous sitosterolaemia or phytosterolaemia)

In patients with 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 tablets do not help patients to lose weight.
How do Ezetimibe 10 mg Tablets work?
Ezetimibe tablets contain the active ingredient ezetimibe, which works by reducing the cholesterol absorbed in the digestive tract.

How are Ezetimibe 10 mg Tablets used?
The patient should always take this medicine exactly as his or her doctor has advised. The patient should check with his/her doctor or pharmacist if unsure.

The patient should continue taking their other cholesterol lowering medicines unless their doctor tells them to stop, if unsure the patient should check with their doctor or pharmacist.

Before starting Ezetimibe tablets, the patient should be on a diet to lower cholesterol and should continue that diet whilst taking Ezetimibe tablets.

The recommended dose in adults and adolescents (10 to 17 years of age):
One Ezetimibe 10 mg tablet by mouth once a day.

If the patient’s doctor has prescribed Ezetimibe tablets along with a statin, both medicines can be taken at the same time. In these cases, the patient should read the dosage instructions in the package leaflet of that particular medicine.

If the patient’s doctor has prescribed Ezetimibe tablets along with cholestyramine or any other bile acid sequestrant (medicines for lowering cholesterol), the patient should take Ezetimibe tablets at least 2 hours before or 4 hours after taking the bile acid sequestrant.

Ezetimibe tablets can be taken:

- At any time of the day, but it is recommended to take them at same time each 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.

This medicine can only be obtained with a prescription.

What benefits of Ezetimibe 10 mg Tablets have been shown in studies?
No additional studies were needed as Ezetimibe 10 mg Tablets is a generic medicine that contains the same active substance in the same concentration as the reference medicine, Ezetrol 10mg Tablets. For this reason, Ezetimibe 10 mg Tablets is expected to be bioequivalent with the reference medicine. Two medicines are considered bioequivalent when they produce the same levels of active substance in the body.

What are the possible side effects of Ezetimibe 10 mg Tablets?
Because Ezetimibe 10 mg Tablets is a generic medicine, its possible side effects are taken as being the same as those of the reference medicine, Ezetrol 10mg Tablets.

For the full list of all side effects reported with Ezetimibe 10 mg Tablets, see Section 4 of the package leaflet available on the MHRA website.

For the full list of restrictions, see the package leaflet.
Why are Ezetimibe 10 mg Tablets approved?
It was concluded that, in accordance with EU requirements, Ezetimibe 10 mg Tablets has been shown to have comparable quality and is considered bioequivalent to Ezetrol 10mg Tablets. Therefore, the MHRA decided that, for Ezetimibe 10 mg Tablets, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Ezetimibe 10 mg Tablets?
A Risk Management Plan (RMP) has been developed to ensure that Ezetimibe 10 mg Tablets is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the package leaflet for this product, 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 10 mg Tablets
On 08 January 2018, Ireland and the UK agreed to grant a Marketing Authorisation for Ezetimibe 10 mg Tablets. Following a subsequent national phase, a Marketing Authorisation was granted on 22 January 2018 in the UK.

The full PAR for Ezetimibe 10 mg Tablets follows this summary.

For more information about treatment with Ezetimibe 10 mg Tablets, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in February 2018.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Introduction</td>
<td>6</td>
</tr>
<tr>
<td>II Quality aspects</td>
<td>6</td>
</tr>
<tr>
<td>III Non-clinical aspects</td>
<td>8</td>
</tr>
<tr>
<td>IV Clinical aspects</td>
<td>10</td>
</tr>
<tr>
<td>V User consultation</td>
<td>10</td>
</tr>
<tr>
<td>VI Overall conclusion, benefit/risk assessment and recommendation</td>
<td>13</td>
</tr>
<tr>
<td>Table of content of the PAR update for MRP and DCP</td>
<td>15</td>
</tr>
</tbody>
</table>
I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Reference Member State (RMS) and Concerned Member States (CMSs) considered that the application for Ezetimibe 10 mg Tablets (PL 34424/0005; UK/H/6438/001/DC) could be approved.

This is a decentralised abridged application submitted under Article 10(1) of Directive 2001/83/EC, as amended, claiming to be a generic medicinal product of the reference product, Ezetrol 10mg Tablets, which was granted a Marketing Authorisation to Merck Sharp & Dohme Limited on 03 April 2003 following a national procedure (PL 00025/0609).

Ezetimibe 10 mg Tablets is a ‘prescription only medicine’ (legal status “POM”) containing the active substance ezetimibe which is indicated for the treatment of:

- **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 nonfamilial) 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) 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.

- **Homzygous 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).

- **Homzygous Sitosterolaemia (phytosterolaemia).** Ezetimibe is indicated as adjunctive therapy to diet for use in patients with homozygous familial sitosterolaemia.

Ezetimibe is a class of lipid-lowering compounds selectively inhibiting the intestinal absorption of cholesterol and phytosterols by targeting the sterol transporter, Niemann-Pick C1-Like 1 (NPC1L1). Although ezetimibe is rapidly absorbed and is extensively metabolized to an active phenolic glucuronide, which reaches the systemic circulation after oral administration, its action is localized at the brush border of the small intestine, leading to a decrease in the delivery of intestinal cholesterol to the liver. This results in a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood. Therefore, Ezetimibe and statins have distinct mechanisms of action that provide complementary cholesterol reduction.

A single bioequivalence study was performed, which compared the pharmacokinetics of the test product Ezetimibe 10 mg Tablet to those of the reference product Ezetrol 10mg Tablets (Merck Sharp & Dohme Limited). The bioequivalence study was carried out in accordance with Good Clinical Practice (GCP).

With the exception of the bioequivalence study, no new clinical or non-clinical studies were conducted which is acceptable given that the application was based on being a generic medicinal product of reference product that has been licensed for over 10 years.

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.

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.

A summary of the pharmacovigilance system and a detailed Risk Management Plan (RMP) have been provided with this application, and these are satisfactory.

The United Kingdom acted as RMS and Ireland was the CMS.

All Member States agreed to grant a Market Authorisation for the above Ezetimibe 10 mg Tablets on 08 January 2018. Following a subsequent national phase, the UK granted a Market Authorisation (PL 34424/0005) for this product on 22 January 2018.
II QUALITY ASPECTS

II.1 Introduction
Ezetimibe 10 mg Tablets contain 10 mg of the active substance ezetimibe. Other ingredients consist of the pharmaceutical excipients lactose monohydrate, croscarmellose sodium, sodium lauryl sulphate, hypromellose, colloidal silicon dioxide, microcrystalline cellulose, hydrogenated castor oil, and sodium stearyl fumarate.

The finished product is packaged in polyvinyl chloride / polyvinylidene chloride transparent film / plain aluminium foil blisters strips which are packaged into cartons containing 28 tablets.

Not all pack sizes may be marketed, however, the marketing authorisation holder has agreed to provide mock-ups of any pack size to the relevant regulatory authorities before marketing.

All primary product packaging complies with the current requirements. Satisfactory specifications and Certificates of Analysis have been provided for all packaging components.

II.2 DRUG SUBSTANCES

Ezetimibe

Chemical Name: (3R,4S)-1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)azetidin-2-one

1-(4-fluorophenyl)-3(R)-[3-(4-fluorophenyl)-3(S)-hydroxypropyl]-4(S)-(4-hydroxyphenyl)-2-azetidinone

Structure:

![Ezetimibe Structure](image)

Molecular Formula: $C_{24}H_{21}F_2NO_3$

Molecular Mass: 409.43

Appearance: White to off-white crystalline powder

Solubility: Freely soluble in methanol and in acetone, soluble in ethanol, practically insoluble in water.
Ezetimibe 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 that comply with the proposed specification are provided.

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 DRUG PRODUCT
Pharmaceutical development
The objective of the development programme was to formulate safe, efficacious, stable, tablets, each containing 10 mg of Ezetimibe, which were comparable in performance to Ezetrol 10mg Tablets (Merck Sharp & Dohme Limited). Suitable pharmaceutical development data have been provided for this application.

All excipients comply with their respective European Pharmacopoeia monographs.

With the exception of lactose monohydrate none of the excipients used contain material of animal or human origin. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

No genetically modified organisms (GMO) have been used in the preparation of this product.

Manufacture of the product
A description and flow-chart of the manufacturing method has been provided.

A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The applicant has confirmed that the manufacturing process will be validated at commercial scale.

Finished Product Specifications
The finished product specification is acceptable. Test methods have been described that have been adequately validated. Batch data that comply with the release specification have been provided. In-house working standards are used, which are compared to European Pharmacopoeia references, where available. Representative Certificates of Analysis have been provided.
Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. The data from these studies support a shelf-life of 36 months for the unopened product, with the storage condition, “Keep in the outer carton in order to protect from moisture.”.

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

II.4 Discussion on chemical, pharmaceutical and biological aspects
It is recommended that a Marketing Authorisation is granted for Ezetimibe 10 mg Tablets.

III NON-CLINICAL ASPECTS

III.1 Introduction
The pharmacodynamic, pharmacokinetic and toxicological properties of the active substance ezetimibe are well-known. No new non-clinical data have been submitted for this application and none are required. 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
No new pharmacology data were submitted and none are required for an application of this type.

III.3 Pharmacokinetics
No new pharmacokinetic data were submitted and none are required for an application of this type.

III.4 Toxicology
No new toxicology data were submitted and none are required for an application of this type.

III.5 Environmental Risk Assessment
Since this product will be used as a substitute for other products that are currently on the market, no increase in environmental exposure is anticipated. An Environmental Risk Assessment (ERA) is, therefore, not deemed necessary. The applicant has provided suitable information to verify that no increase in the exposure of the environment to the active ingredient is to be expected.

III.6 Discussion on non-clinical aspects
It is recommended that a Marketing Authorisation is granted for Ezetimibe 10 mg Tablets.

IV CLINICAL ASPECTS

IV.1 Introduction
No new clinical 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.
IV.2 Pharmacokinetics

In support of the application, the Marketing Authorisation Holder has submitted results from the following bioequivalence study:

Open-label, balanced, randomized, single-dose, two-treatment, two-sequence, two-period, crossover, oral bioequivalence study of comparing the pharmacokinetics of the test product Ezetimibe 10 mg Tablets (Key Pharmaceuticals Ltd.) and Ezetrol 10 mg Tablets (Merck Sharp & Dohme Limited, UK) in healthy, adult subjects under fasting conditions.

After an overnight fast of 10 hours each subject received a single dose of the test formulation (1 x 10 mg) or a single dose of the reference medicine (1 x 10 mg), administered with 240mL of drinking water. Blood samples were collected before dosing and up to and including 72 hours after dosing.

A washout period of 14 days was kept between each dosing period.

Summary statistics for pharmacokinetic parameters for the test and reference product are shown in the tables below:

Table 1. Pharmacokinetic parameters for Ezetimibe (unconjugated) obtained by a Non-Compartmental Model (N = 38) (non-transformed values; arithmetic mean ± SD, \( t_{\text{max}} \) median, range)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AUC(_{0-t}) ng/ml/h</th>
<th>AUC(_{0-\infty}) ng/ml/h</th>
<th>C(_{\text{max}}) ng/ml</th>
<th>( t_{\text{max}} ) h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>69.3182 ± 38.25036</td>
<td>93.0349 ± 64.67668</td>
<td>4.5101 ± 2.15231</td>
<td>6.836 ± 4.4106</td>
</tr>
<tr>
<td>Reference</td>
<td>67.6534 ± 32.80137</td>
<td>83.6428 ± 41.24223</td>
<td>4.8697 ± 2.64193</td>
<td>6.178 ± 3.1777</td>
</tr>
<tr>
<td>*Ratio (90% CI)</td>
<td>97.00 (86.66, 108.57)</td>
<td>N/A</td>
<td>95.23 (85.91, 105.56)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

| **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. (Only for immediate release products)
| **AUC\(_{0-72h}\)** | Area under the plasma concentration curve from administration to last observed concentration at time \( t \), where the concentration at 72 h is quantifiable. In studies with a sampling period of 72 h, AUC\(_{0-72h}\) can be reported instead of AUC\(_{0-t}\) when \( AUC_{0-72h} \) is reported instead of AUC\(_{0-t}\).
| **C\(_{\text{max}}\)** | Maximum plasma concentration.
| **\( t_{\text{max}} \)** | Time until C\(_{\text{max}}\) is reached.

*ln-transformed values
Table 2. Pharmacokinetic parameters for total Ezetimibe (ezetimibe + ezetimibe glucuronide) obtained by a Non-Compartmental Model (N = 38) (non-transformed values; arithmetic mean ± SD)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AUC(_{0-t}) ng/ml/h</th>
<th>AUC(_{0-\infty}) ng/ml/h</th>
<th>C(_{\text{max}}) ng/ml</th>
<th>t(_{\text{max}}) h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>735.8830 ± 359.98696</td>
<td>813.9642 ± 439.26576</td>
<td>87.9888 ± 46.46178</td>
<td>14.9173 ± 9.21379</td>
</tr>
<tr>
<td>Reference</td>
<td>742.5084 ± 240.53840</td>
<td>807.1618 ± 278.95902</td>
<td>91.6558 ± 39.19911</td>
<td>14.4581 ± 7.78436</td>
</tr>
</tbody>
</table>

*Ratio (90% CI) 93.96 (87.16, 101.30), N/A 91.54 (80.45, 104.15), N/A

AUC\(_{0-t}\) Area under the plasma concentration curve from administration to last observed concentration at time t. AUC\(_{0-72h}\) can be reported instead of AUC\(_{0-t}\) in studies with a sampling period of 72 h, and where the concentration at 72 h is quantifiable. Only for immediate release products.

AUC\(_{0-\infty}\) Area under the plasma concentration curve extrapolated to infinite time. AUC\(_{0-\infty}\) does not need to be reported when AUC\(_{0-72h}\) is reported instead of AUC\(_{0-t}\).

C\(_{\text{max}}\) Maximum plasma concentration

Conclusion
The 90% confidence intervals of the test/reference ratio for AUC and C\(_{\text{max}}\) values for ezetimibe and ezetimibe glucuronide 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**). Based on the data provided the applicant’s test product, Ezetimibe 10 mg Tablets can be considered bioequivalent to the reference product, Ezetrol 10 mg Tablets (Merck Sharp & Dohme Limited).

IV.3 Pharmacodynamics
No new pharmacodynamic data were submitted and none are required for an application of this type.

IV.4 Clinical Efficacy
No new data on efficacy have been submitted and none are required for an application of this type.

IV.5 Clinical Safety
No new data on clinical safety have been submitted and none are required for an application of this type.

IV.6 Risk Management Plan (RMP)
The marketing authorisation holder has submitted an 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 10 mg Tablets.
A summary of safety concerns, as approved in the RMP, are listed below:

### Table 1. Summary of safety concerns

<table>
<thead>
<tr>
<th>Important identified risks</th>
<th>Hypersensitivity to active substance or any other ingredient of the medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Skeletal muscle pain / myopathy and rhabdomyolysis</td>
</tr>
<tr>
<td></td>
<td>Abnormal liver function</td>
</tr>
<tr>
<td></td>
<td>Drug interactions with ciclosporin and Drug interaction with warfarin, another coumarin anticoagulant or fluindione.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Important potential risks</th>
<th>Cholelithiasis/cholecystitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk of pancreatitis (inflammation of the pancreas)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Missing information</th>
<th>Pregnancy and lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paediatric population- Limited clinical trial experience in children age 10-17 years old beyond 1 year and in children 6-10 years old beyond 12 weeks. No clinical trial experience in children less than 6 years of age.</td>
</tr>
</tbody>
</table>

Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.

### IV.7 Discussion of the clinical aspects

It is recommended that a Marketing Authorisation is granted for Ezetimibe 10 mg Tablets.

### V USER CONSULTATION

A user consultation with target patient groups on the package leaflet has been performed and the results submitted in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package 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.

### VI. OVERALL CONCLUSION AND BENEFIT RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Bioequivalence has been demonstrated between the applicant’s product and the reference product. Extensive clinical experience with ezetimibe is considered to have demonstrated the therapeutic value of the compound.

The benefit-risk is, therefore, considered to be positive.

### PRODUCT LITERATURE

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 current labelling is presented below:
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  
(Type II variations, PSURs, commitments)

<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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>