Public Assessment Report

Decentralised Procedure

Mometasone Furoate 0.1% w/w Cream

(mometasone furoate)

Procedure No: UK/H/3209/001/DC

UK Licence No: PL 17507/0111

Auden Mckenzie (Pharma Division) Ltd
LAY SUMMARY
Mometasone Furoate 0.1% w/w Cream
(mometasone furoate)

This is a summary of the public assessment report (PAR) for Mometasone Furoate 0.1% w/w Cream (PL 17507/0111; UK/H/3209/001/DC). It explains how Mometasone Furoate 0.1% w/w Cream 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 Mometasone Furoate 0.1% w/w Cream, patients should read the package leaflet or contact their doctor or pharmacist.

What is Mometasone Furoate 0.1% w/w Cream and what is it used for?
The application for Mometasone Furoate 0.1% w/w Cream was submitted as a hybrid medicine. Assessment of the application concluded that the cream is similar to a reference medicine containing same active substance (mometasone furoate) in the same dose.

The reference medicine already authorised in the UK is Elocon 0.1%w/w Cream (Merck Sharp &Dohme Limited; PL 00025/0577).

Mometasone Furoate 0.1% w/w Cream is used to reduce redness and itchiness caused by certain skin problems such as psoriasis (skin disease in which itchy, scaly, pink patches develop on the elbows, knees, scalp and other parts of the body), excluding widespread plaque psoriasis, and some types of dermatitis (a condition brought on by the skin reacting to outside agents e.g. detergents causing the skin to become red and itchy).

How is Mometasone Furoate 0.1% w/w Cream used?
Usually a small amount of cream is gently applied to the affected area of the skin once daily. Mometasone Furoate 0.1% w/w Cream should be used as advised by a doctor and should not be used for more than 5 days.

The use of Mometasone Furoate Cream in children should be supervised by a doctor. This medicinal product is not recommended for use in children under the age of 6.

Mometasone Furoate 0.1% w/w Cream can only be obtained on prescription from a doctor.

For further information on how Mometasone Furoate 0.1% w/w Cream is used, please see the Summary of Product Characteristics and package leaflet available on the MHRA website.

How does Mometasone Furoate 0.1% w/w Cream work?
Mometasone Furoate 0.1% w/w Cream contains the active substance, mometasone furoate, which belongs to a group of medicines called topical corticosteroids and is
classified as a “potent corticosteroid”. This medicinal product reduces the redness and itchiness caused by certain skin problems.

What benefits of Mometasone Furoate 0.1% w/w Cream has been shown in studies?
Because the application for Mometasone Furoate 0.1% w/w Cream was submitted as a hybrid application and is considered to be therapeutically equivalent to the reference product, Elocon 0.1% w/w Cream, its benefits and risks are taken as being the same as those of the reference medicine.

What are the possible side effects from Mometasone Furoate 0.1% w/w Cream?
Like all medicines, Mometasone Furoate cream can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Mometasone Furoate 0.1% w/w Cream, see section 4 of the package leaflet.

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

Why is Mometasone Furoate 0.1% w/w Cream approved?
The MHRA decided that the benefits of Mometasone Furoate 0.1% w/w Cream are greater than its risks and recommended that it be approved for use.

What measures are being taken to ensure the safe and effective use of Mometasone Furoate 0.1% w/w Cream?
A Risk Management Plan has been developed to ensure Mometasone Furoate 0.1% w/w Cream is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Mometasone Furoate 0.1% w/w Cream, 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 Mometasone Furoate 0.1% w/w Cream
The Republic of Ireland and the UK agreed to grant a Marketing Authorisation for Mometasone Furoate 0.1% w/w Cream on 25th April 2012. A Marketing Authorisation was granted in the UK on 20th June 2012.

For more information about taking Mometasone Furoate 0.1% w/w Cream, read the Patient Information Leaflet (PIL), or contact your doctor or pharmacist.

The full PAR for Mometasone Furoate 0.1% w/w Cream follows this summary.

This summary was last updated in May 2015.
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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK and Republic of Ireland considered that the application for Mometasone Furoate 0.1% w/w Cream (PL 17507/0111; UK/H/3209/001/DC) is approvable. The product is a prescription-only medicine (POM) indicated for the treatment of inflammatory and pruritic manifestations of psoriasis (excluding widespread plaque psoriasis) and atopic dermatitis.

This application was submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS) and Republic of Ireland as Concerned Member State (CMS). The application was made under Article 10.3 of Directive 2001/83/EC, as amended, as a hybrid application. The reference medicinal product for this application is Elocon 0.1% w/w Cream, which was originally authorised to Schering-Plough Limited (PL 00201/0117) on 19th November 1991. This reference license underwent a change of ownership procedure to Merck Sharp & Dohme Limited (PL 00025/0577) on 22nd December 2010.

The active ingredient, mometasone furoate, is a potent topical corticosteroid. Mometasone furoate exhibits marked anti-inflammatory activity and marked anti-psoriatic activity in standard animal predictive models.

No new non-clinical data have been submitted, which is acceptable given that this is a hybrid application based on an originator product that has been in clinical use for over 10 years.

To support the application, the Marketing Authorisation Holder submitted three clinical studies. These studies included a pilot study to validate the vasoconstriction assay, a pivotal therapeutic study to demonstrate equivalence of the vasoconstriction response between the test product Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma Division] Ltd, UK) and the reference product Elocon Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation) and a cumulative irritation study to demonstrate comparable safety between the test product Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma Division] Ltd, UK) and the reference product Elocon Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation). During product development, Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma Division] Ltd, UK) was the name used for Mometasone Furoate 0.1% w/w Cream (Auden Mckenzie [Pharma Division] Ltd, UK). The studies were carried out in accordance with Good Clinical Practice (GCP).

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.

The RMS and CMS considered that the application could be approved at the end of procedure (Day 150) on 25 April 2012. After a subsequent national phase, a licence was granted in the UK on 20 June 2012.
II QUALITY ASPECTS

DRUG SUBSTANCE

INN: Mometasone furoate

Structure:

Molecular formula: $\text{C}_{27}\text{H}_{30}\text{Cl}_{2}\text{O}_{6}$
Molecular mass: 521.4 g/mol

Appearance: Mometasone furoate is a white or off-white powder.

Solubility: Practically insoluble in water, slightly soluble in ethanol (96 percent), soluble in acetone and in methylene chloride.

Mometasone furoate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance, mometasone furoate, are covered by a European Directorate for the Quality of Medicines Healthcare (EDQM) Certificate of Suitability.

DRUG PRODUCT

Other ingredients consist of the pharmaceutical excipients, namely hexylene glycol, stearyl alcohol and macrogol ceteareth-20, white beeswax, propylene glycol monopalmitostearate, titanium dioxide (E171), aluminium starch octenylsuccinate, dilute phosphoric acid, white soft paraffin, and purified water.

With the exception of stearyl alcohol and macrogol ceteareth-20, aluminium starch octenylsuccinate and hexylene glycol, all excipients comply with their respective European Pharmacopoeia monographs. Stearyl alcohol and ceteareth-20, and aluminium starch octenylsuccinate are controlled to suitable in-house specifications. Hexylene glycol is compliant with the United States Pharmacopeia - National formulary (USP-NF) specification. Satisfactory Certificates of Analysis have been provided for all excipients.

None of the excipients contain materials of animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of these excipients.

Pharmaceutical Development

The objective of the development programme was to formulate a stable topical preparation that was comparable in performance to the reference product Elocon 0.1% Cream (Merck Sharp & Dohme Limited, UK).

Suitable pharmaceutical development data have been provided for this application.
Comparative physico-chemical, *in-vitro* diffusion and impurity profiles have been provided for this product and the reference product.

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

**Control of Finished Product**
The finished product specification proposed is acceptable. The test methods have been described and have been adequately validated. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for all working standards used.

**Container-Closure System**
The finished product is supplied in collapsible aluminium tubes internally coated with an epoxy resin based lacquer and closed with polypropylene caps. The tubes are packaged with the Product Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 30 g and 100 g tubes.

Not all pack sizes may be marketed.

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

**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 for the product stored in the unopened tubes has been set. The shelf-life after first opening a tube is 3 months. The storage instructions for the product are “Store below 30°C.”

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

**Therapeutic Equivalence**
Bioequivalence studies are not necessary to support this application. For products for local application intended to act without systemic absorption, the approach to determine equivalence on systemic measurements is not applicable and pharmacodynamic or comparative clinical studies are required. The applicant has submitted a pilot and pivotal studies to establish therapeutic equivalence of the vasoconstriction response between the proposed product and the reference product, and a third cumulative irritation study to demonstrate comparable safety between the test and reference products. The studies are discussed in Section IV, Clinical Aspects.
Summary of Product Characteristics (SmPC), Product Information Leaflet (PIL), Labels
The SmPC, PIL and labels are satisfactory from a pharmaceutical perspective.

Marketing Authorisation Application (MAA) Form
All aspects of the MAA form are satisfactory from a pharmaceutical perspective.

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

Conclusion
The grant of a Marketing Authorisation is recommended.
III NON-CLINICAL ASPECTS
The pharmacodynamic, pharmacokinetic and toxicological properties of mometasone furoate are well-known. As mometasone furoate is a widely used, well-known active substance, no new non-clinical data have been submitted and none are required.

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

As this product is intended for substitution with a product that is already marketed, no increase in environmental burden is anticipated and no Environmental Risk Assessment is necessary.

The grant of a Marketing Authorisation is recommended.
IV  CLINICAL ASPECTS

Clinical Pharmacology
The clinical pharmacology of mometasone furoate is well-known. With the exception of the therapeutic equivalence studies detailed below, no new pharmacodynamic or pharmacokinetic data are provided or required for this application.

Pharmacodynamic studies
In accordance with CHMP/EWP/21441/06 – “Questions and Answers on Guideline: Clinical investigation of corticosteroids intended for use on the skin”, vasoconstriction assays can be used in place of therapeutic equivalence studies in case where the composition of the proposed and reference products is very similar.

In support of the application, the Marketing Authorisation Holder submitted a pilot study to validate the vasoconstriction assay method, a pivotal pharmacodynamic vasoconstrictor response study to demonstrate equivalence of the test product (Mometasone Furoate 0.1% w/w Cream; Auden Mckenzie [Pharma Division] Ltd) to the reference product (Elocon Cream 0.1% w/w; manufactured by Schering-Plough Limited, Corporation) in healthy subjects and a third cumulative irritation study to demonstrate comparable safety between the test and reference products.

Pilot Study
A single exposure, dose-ranging study to evaluate the vasoconstriction activity of topically delivered mometasone furoate cream 0.1% in normal skin in healthy adult subjects: A dose ranging study

Methodology
The study design, volunteer selection criteria, study restrictions, clinical methodology, validation of assay precision, data analysis and modelling of the pilot dose-duration study were all in line with the FDA guidance.

The study consisted of two parts:
Part A was to validate the vasoconstriction assay precision and reproducibility of the test facility’s technique and instrumentation.

Part B was to determine the optimal derived ED$_{50}$ on vasoconstriction for the duration of application to be used in the pivotal study. This dose would then identify the three doses to be included in the pivotal study.

In Part A, subjects had four 4 cm$^2$ untreated sites on one forearm measured by chromometer to assess reproducibility and precision.

In Part B subjects had eight 4 cm$^2$ sites on both forearms treated with Elocon® Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation) for different durations of dose application ranging from 30-360 minutes, in duplicate. The dose of cream applied was 5 µL/cm$^2$ (20 µL/site). Two sites on each fore-arm remained untreated to serve as control sites. All sites remained un-occluded after application. Staggered application with synchronized removal technique was used. Dose removal was by using three sequential swabs with two damp followed by one dry swab, where each swab wiped the test site three times while wiping across the entire test area.
Vasoconstriction response (skin blanching) was evaluated by chromameter at pre-dose, and after dose removal at 11 time points up to 24 hours.

**Statistical analysis**

Vasoconstriction data analyses were conducted as described in the FDA Guidance. Chromameter L*a*b*-a values for each time point and site were corrected for baseline reading and by the untreated site reading. Negative Area Under the Effect Curve (AUEC) values for the duration of 24 hours post dose removal were calculated from the final corrected (a*) values using the trapezoidal rule. Maximum effect (E\text{max}) and ED\text{50} were determined using software specifically designed for population modelling.

**Results**

The results are presented below:

![Graph showing the means negative a* areas (0-24 h Areas) under the effect curve for dose duration times 30-360 minutes (log-normal model)](image)

Results of the Modelling Analyses Performed on the Negative AUEC Values (using log-normal distribution)

<table>
<thead>
<tr>
<th>E\text{max}</th>
<th>ED\text{50} (Minutes)</th>
<th>AIC</th>
<th>BIC</th>
<th>OBJ</th>
<th>Negative Log Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>40.44</td>
<td>137.92</td>
<td>3.8033</td>
<td>3.8219</td>
<td>965.15</td>
<td>636.96</td>
</tr>
</tbody>
</table>

**Safety results:** No adverse events (AEs) were reported over the course of the study.

**Conclusion on the pilot study**

The curve fit for mean AUC of vasoconstriction versus dose-duration showed a response towards a plateau by 6 hours and analysis validated the model for evaluating therapeutic equivalence. Based on the ED\text{50} of 137.92, an appropriate dose to be used in the pivotal therapeutic equivalence study was 140 minutes, with a D\text{1} of 70 minutes
and a $D_2$ of 280 minutes.

**Pivotal Study:**

**A single-blind, single-exposure study to compare the dose duration vasoconstriction response of the test product Mometasone Furoate 0.1% w/w Cream, and the test product Elocon Cream 0.1% w/w in normal skin in healthy adult male and female subjects.**

Subjects who had demonstrated a visual vasoconstriction score of 1 or greater during standard screening for vasoconstrictive responsiveness were enrolled. Subjects had a total of ten 4 cm$^2$ sites demarcated on each forearm, of which eight 4 cm$^2$ sites on each forearm were dosed with two formulations which contained mometasone furoate 0.1% cream. Two sites on each forearm remained untreated to serve as control sites. Dose durations of $D_1$ (70 minutes), $D_2$ (280 minutes), and $ED_{50}$ (140 minutes) were based on values for the reference product, Elocon® Cream 0.1% w/w, as determined in the dose ranging pilot study.

The reference product, Elocon Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation) was applied to two sites per arm for the $D_1$, $ED_{50}$, and $D_2$ durations (six sites). The test product Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma Division] Ltd) was dosed on two sites per arm using the same $ED_{50}$ dose duration. All sites remained un-occluded after application.

The dose of cream applied at each site was 5 µL/cm$^2$ (20 µL/site) and the technique of staggered dosing with synchronised removal was used as in the pilot study. Dose removal was by using three sequential swabs with two damp followed by one dry swab, where each swab wiped the test site three times while wiping across the entire test area. Vasoconstriction response was evaluated by chromameter at pre-dose and for 24 hours after dose removal at 11 time points (1 to 24 hours).

**Statistical analysis**

Vasoconstriction data analyses were conducted as described in the FDA Guidance. Chromameter L*a*b*-a values for each time point and site were corrected for baseline reading and by the untreated site reading.

A blinded sample size re-estimation method, adequately supported by published literature was undertaken; this was considered acceptable.

Only the data of ‘detectors’, i.e., individual subjects whose negative Area Under the Effect Curve (AUEC) values at $D_1$ and $D_2$ were both positive and that met the dose duration-response criterion below, were included in the final analysis. The dose duration-response criterion was:

$$\frac{AUEC \_ at \_ D_2}{AUEC \_ at \_ D_1} \geq 1.25$$

A 90% confidence interval (CI) about the ratio of the mean test value to mean reference value was calculated for average AUEC response according to Locke’s method.
Results
The results are presented below:

Means of Negative AUEC (0-24 h), Ratio of Means, and 90% Confidence Interval (Locke) of Mometasone Furoate Cream 0.1%

<table>
<thead>
<tr>
<th>Mean Negative AUEC (0-24 h)</th>
<th>% Ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Product</td>
<td>Reference Product</td>
<td></td>
</tr>
<tr>
<td>29.49</td>
<td>26.05</td>
<td>113.20</td>
</tr>
</tbody>
</table>

Treatment A: Mometasone Furoate 0.1% Cream
Treatment B: Elocon® Cream 0.1% w/w

Mean corrected a* Values (0-24 h) for Mometasone Furoate Cream 0.1%

Safety Results: No serious adverse events (SAEs) were reported over the course of this study and no subject was discontinued due to an adverse event (AE).

Overall, the most common AE was headache, which was reported on one occasion by 3 (2.5%) subjects. Two headaches were considered mild and one headache was considered moderate in intensity; all were considered to be unlikely or not related to the study treatments.

Conclusion
The pivotal study is generally in line with the FDA guidelines which are accepted in Europe. Minor deviations such as dose-removal and the number of sites of drug administration in each arm (eight as opposed to recommended six in the guidance) is considered acceptable as replication of sites for D1 and D2 will only enhance the replication design and reliability of results.
The 90% confidence intervals of the test/reference ratio for the means of negative AUEC\(_{(0-24hr)}\) lie within the equivalence interval of 80.00-125.00%. Thus the data support the claim that the test product Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma Division] Ltd) is therapeutically equivalent to Elocon Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation).

**Cumulative Irritation Study**

A randomized, single-centre, phase I study to evaluate the 21-day cumulative irritation potential of mometasone furoate cream 0.1% in normal skin in healthy adult subjects.

A standard 21-day, cumulative irritation methodology was used to evaluate the skin sensitization properties of the test product Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma Division] Ltd) in comparison with the reference product Elocon Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation). A positive (known irritant of human skin – sodium lauryl sulphate [SLS] 0.1% w/v solution) and a negative control (placebo – Sterile water for injection applied on the skin) arm were used for assay validity and sensitivity.

Each subject received 21 consecutive daily applications of 0.2ml of each test article to four test sites on the outside of the upper arms under occluded conditions. The test articles were applied to the same sites every 24 hours (± 1 hour) for a total of 21 applications. The mean cumulative irritation scores at the same site measured daily between 20 and 40 minutes after removal on days 2 through 22 were measured.

Skin reactions were scored using pre-defined scales.

If the degree of irritation for a given test article was such that a new application of the test article could not be applied to the same site, the product was discontinued from further application at that site. The test site was still observed and scored at each subsequent visit; however, the last score observed prior to test article discontinuation was carried forward and used in the primary analysis.

The primary objective was to determine and compare the mean cumulative irritation score (as the sum of all combined “Dermal Response” and “Other Effects” scores) from 21 consecutive daily applications of the reference product (Elocon Cream 0.1% w/w) to the cumulative irritation produced by test product (Mometasone Furoate 0.1% Cream) and thereby determine whether the test product was non-inferior to Elocon® in terms of cumulative irritation.

The relevant hypotheses were:

\[ H_0: \text{median}_T – 1.25\text{median}_R > 0 \ (\text{not non-inferior}) \]
\[ H_1: \text{median}_T – 1.25\text{median}_R \leq 0 \ (\text{non-inferior}) \]

To demonstrate non-inferiority of the test product compared to the reference product with regard to the cumulative irritation scores, the upper bound of the one-sided 95% confidence interval (CI) of the median cumulative irritation score for the test product (median\(_T\)) minus the median of 1.25 times the cumulative irritation score for the reference product (median\(_R\)) must be less than or equal to 0.
A 95% bootstrap CI of the median difference between test (Treatment B) and reference (Treatment A) was used for evaluating non-inferiority. In addition, the comparison of Treatment C (positive irritant control) and Treatment D (negative irritant control) was performed in an identical manner.

**Results**
The results are present below:

### Cumulative Dermal Irritation Scores

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment A (Reference Cream)</td>
<td>13.00</td>
<td>2.80</td>
<td>12.00</td>
</tr>
<tr>
<td>Treatment B (Test Cream)</td>
<td>13.21</td>
<td>3.04</td>
<td>13.00</td>
</tr>
<tr>
<td>Treatment C (Positive Control)</td>
<td>45.41</td>
<td>9.46</td>
<td>45.00</td>
</tr>
<tr>
<td>Treatment D (Negative Control)</td>
<td>10.15</td>
<td>3.29</td>
<td>10.00</td>
</tr>
</tbody>
</table>

The following table summarizes the bootstrapping confidence intervals based on the cumulative irritation scores (Test – 1.25*Reference):

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Median Difference</th>
<th>Upper Bound of 95% Bootstrap Confidence Limit of the Median Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment B (Mometasone Furoate 0.1% Cream) vs Treatment A (Elocon® Cream 0.1%)</td>
<td>-2.875</td>
<td>-2</td>
</tr>
<tr>
<td>Treatment C (Positive Irritant Control) vs Treatment D (Negative Irritant Control)</td>
<td>30.625</td>
<td>34.3</td>
</tr>
</tbody>
</table>

**Safety:** Five subjects experienced a total of 13 mild and 1 moderate adverse event. The most common AE reported was application site pruritus (3 cases in 2 subjects for the positive control considered related to the SLS and 1 case for the negative control, also considered to be related) and nausea (occurred in 2 subjects, considered not related).

Application site pain occurred on two occasions in the same subject (1 with the positive control, 1 with the negative control). Both cases were considered to be related to treatment.

Arthralgia, diarrhoea, dizziness, headache, nasopharyngitis, and vomiting occurred on one occasion in 1 subject each; all were considered unlikely or not related to the study treatment.

**Conclusion of the cumulative irritation study**
The test product (Mometasone Furoate 0.1% Cream (Auden Mckenzie [Pharma}
Division] Ltd) showed a comparable, low cutaneous irritation score with that of both placebo and the reference product Elocon Cream 0.1% w/w (manufactured by Schering-Plough Limited, Corporation).

The results of the study support the claim that the test product Mometasone Furoate Cream, 0.1% is non-inferior to the reference product Elocon® Cream 0.1% in terms of irritation.

**Safety**
With the exception of the data from the above pilot study, pivotal therapeutic equivalence study and cumulative irritation study, no new clinical data were submitted and none were required. The safety data collected during the study showed that the test and reference product had a comparable tolerability. No new, unexpected adverse events occurred during the clinical studies.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels**
The SmPC, PIL and labels are acceptable from a clinical perspective. The SmPC is consistent with that for the reference product. The PIL is consistent with the details in the SmPC and in line with the current guidelines. The labelling is in-line with the current guidelines.

**Clinical Overview**
The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.
**Risk Management Plan (RMP)**

The Marketing Authorisation Holder (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 Mometasone Furoate 0.1% w/w Cream.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, is listed below:

**Summary table of risk minimisation measures:**

<table>
<thead>
<tr>
<th>Safety concern</th>
<th>Routine risk minimisation activities sufficient?</th>
<th>If yes, provide description of routine activity and justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site pain, application site reactions,</td>
<td>Yes</td>
<td>SmPC Section 4.4 (Special warnings and precautions for use) and Section 4.8 (Undesirable effects), PIL Section 2</td>
</tr>
<tr>
<td>Skin irritation or sensitisation, Burning sensation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contra-indicated in ulcerated skin (with wounds): rosacea (a skin condition affecting the face) acne, skin atrophy (thinning of the skin) , dermatitis around the mouth, napkin eruptions</td>
<td>Yes</td>
<td>SmPC Section 4.3 (Contraindications) and Section 2</td>
</tr>
<tr>
<td>Contraindicated in the following conditions: Bacterial Infection (e.g.</td>
<td>Yes</td>
<td>SmPC Section 4.3 (Contraindications) and Section 2</td>
</tr>
</tbody>
</table>
## Conclusion

The grant of a Marketing Authorisation is recommended.

<table>
<thead>
<tr>
<th>Potential risk</th>
<th>Supplementary Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral infection (e.g., herpes simplex, herpes zoster, chickenpox, verrucae vulgares, condylomata acuminata and molluscum contagiosum)</td>
<td>Yes SmPC Section 4.4 and PIL Section 2</td>
</tr>
<tr>
<td>Parasitological and fungal (e.g., candida or dermatophyte) infections, varicella, tuberculosis, syphilis or post-vaccine reactions Folliculitis (inflammation and/or infection of the hair follicles)</td>
<td>Yes SmPC Section 4.4 and PIL Section 2</td>
</tr>
<tr>
<td>Excess of corticosteroid (Cushing's syndrome), High glucose level (hyperglycemia), and Abnormal high level of glucose in urine (glucosuria)</td>
<td>Yes SmPC Section 4.4 and PIL Section 2</td>
</tr>
<tr>
<td>Glucocorticoid insufficiency</td>
<td>Yes SmPC Section 4.4 and PIL Section 2</td>
</tr>
<tr>
<td>Local and systemic toxicity</td>
<td>Yes SmPC Section 4.4 (Contra-Indications) and PIL Section 2</td>
</tr>
<tr>
<td>Relapse of psoriasis, risk of centralised pastular psoriasis</td>
<td>Yes SmPC Section 4.4 (Contra-Indications) and PIL Section 2</td>
</tr>
<tr>
<td>Dermatitis with intense redness, stinging and burning</td>
<td>Yes SmPC Section 4.4 (Contra-Indications) and PIL Section 2</td>
</tr>
<tr>
<td><strong>Important potential risks</strong></td>
<td></td>
</tr>
<tr>
<td>Glaucoma simplex (increased pressure within the eye), Subcapsular cataract (decrease in vision)</td>
<td>Yes SmPC Section 4.4 and PIL Section 3</td>
</tr>
<tr>
<td>Caution should be exercised when used in pregnant women</td>
<td>Yes SmPC Section 4.6 and PIL Section 2</td>
</tr>
<tr>
<td>Use in nursing mothers</td>
<td>Yes SmPC Section 4.6 and PIL Section 2</td>
</tr>
<tr>
<td>Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios.</td>
<td>Yes SmPC Section 4.4 and PIL Section 2</td>
</tr>
</tbody>
</table>

### Missing information

Safety and efficacy of Mometasone Furoate in paediatric patients below 6 years of age Yes SmPC Section 4.4 and PIL Section 2
V. User consultation
The 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 patient information leaflet (PIL) was English.

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 AND BENEFIT/RISK ASSESSMENT AND RECOMMENDATION
QUALITY
The important quality characteristics of Mometasone Furoate 0.1% w/w Cream 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. As the pharmacokinetics, pharmacodynamics and toxicology of mometasone furoate are well-known, no additional data were required.

CLINICAL
With the exception of the data submitted in the pilot study and pivotal pharmacodynamic study, no new clinical data were submitted and none are required for this type of application.

Therapeutic equivalence has been demonstrated between the applicant’s Mometasone Furoate 0.1% w/w Cream and the reference product Eloccon Cream 0.1% w/w (Merck, Sharp & Dohme, UK).

SAFETY
The safety profile of mometasone furoate is well-known. With the exception of the safety data generated during the clinical studies, no new safety data were submitted and none are required for applications of this type. No new or unexpected safety issues arose during the clinical studies.

PRODUCT LITERATURE
The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product, where appropriate, and consistent with current guidelines.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with mometasone furoate is considered to have demonstrated the therapeutic value of the product. The benefit/risk balance is, therefore, considered to be positive.
Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report

The following table lists some non-safety updates to the Marketing Authorisation for this product that have been approved by the MHRA since the product was first licensed. The table includes updates that are detailed in the annex to this PAR. This is not a complete list of the post-authorisation changes that have been made to this Marketing Authorisation.

<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>To update the SmPC in line with changes agreed during the mutual recognition procedure. Sections 4.1, 4.2, 4.4, 4.8 and 6.1 have been updated. In addition, the risk management plan has been updated accordingly. Consequently, the label and PIL has been updated.</td>
<td>UK/H/320/001/IB/012/G</td>
<td>SmPC, PIL and label</td>
<td>05/12/2014</td>
<td>01/04/2015</td>
<td>Approval</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Annex 1

Reference: PL 17507/0111-0019

Product: Mometasone Furoate 0.1% w/w Cream

MAH: Auden Mckenzie (Pharma Division) Ltd

Active Ingredient: Mometasone furoate

Reason:
To update the SmPC in line with changes agreed during the mutual recognition procedure (MRP). Sections 4.1, 4.2, 4.4, 4.8 and 6.1 have been updated. In addition, the risk management plan (RMP) has been updated accordingly. Consequently, the label and PIL has been updated.

Supporting Evidence
The applicant has submitted updated sections of the SmPC, leaflet and label.

Evaluation
The amended sections of the SmPC, the leaflet and label mock-ups are satisfactory.

Conclusion
The variation was approved on 1st April 2015 and the updated SmPC fragments, the PIL and labelling have been incorporated into this Marketing Authorisation. The proposed changes are acceptable.
SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) - Updated

Following approval of the variation on 1st April 2015 the SmPC was updated. In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) for products that have been granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET (PIL) - Updated

Following approval of the variation on 1st April 2015 the PIL was updated. In accordance with Directive 2010/84/EU the Patient Information Leaflet (PIL) for products that have been granted Marketing Authorisations at a national level are available on the MHRA website.
Mometasone Furoate 0.1% w/w Cream

1 g of cream contains 1 mg of mometasone furoate (0.1% w/w).

Please read the enclosed leaflet before use. For cutaneous use. For external use only.

Do not store above 30°C. This medicine should be disposed of 3 months after first opening.

Medicinal product subject to medical prescription.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

POM
Mometasone Furoate 0.1% w/w Cream

1 g of cream contains 1 mg of mometasone furoate (0.1% w/w).

See leaflet for further information.

Do not store above 30°C. This medicine should be dispensed 3 months after first opening.

Medical product subject to medical prescription.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

For external use only.

For consultation use.

PAR Mometasone Furoate 0.1% w/w Cream

UK/H/3209/001/DC
Mometasone Furoate 0.1% w/w Cream

1 g of cream contains 1 mg of mometasone furoate (0.1% w/w).

Please read the bridged leaflet before use.

For external use only.

Do not store above 30°C. Medicinal product subject to medical prescription. This medicine should be disposed of 3 months after first opening. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

Pl.No. TN0709111 PA.No. 1850181
GlaxoSmithKline Healthcare UK Limited (Pharmaco Division)
Midlands House, Bury Street, Reading, Berkshire, RG1 7PL, UK.

Mometasone Furoate 0.1% w/w Cream

30 g