Public Assessment Report

DCPAR

Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension

(Mometasone Furoate Monohydrate)

Procedure No: UK/H/6175/001/DC

UK Licence Numbers: PL 00289/2037

TEVA UK Limited
LAY SUMMARY

Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension
(Mometasone Furoate Monohydrate)

This is a summary of the Public Assessment Report (PAR) for Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension (UK/H/6175/001/DC; PL 00289/2037). It explains how Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension 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 Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension.

This product will be referred to as Mometasone Furoate Suspension in this lay summary for ease of reading.

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

What is Mometasone Furoate Suspension and what is it used for?
Mometasone Furoate Suspension is a ‘generic medicine’. This means that it is similar to a ‘reference medicine’ already authorized in the European Union (EU) called Nasonex 50 micrograms/actuation Nasal Spray Suspension (PL 00025/0587, Merck Sharp & Dohme Ltd).

Mometasone Furoate Nasal Spray is used in adults to treat the symptoms of hay fever (also called seasonal allergic rhinitis).

Hay fever, which occurs at certain times of the year, is an allergic reaction caused by breathing in pollen from trees, grasses, weeds and also moulds and fungal spores. Mometasone furoate Nasal Spray reduces the swelling and irritation in the nose and thereby relieving sneezing, itching and a blocked-up or runny nose caused by hay fever.

How does Mometasone Furoate Suspension work?
Mometasone furoate is a corticosteroid which has an anti-inflammatory action, reducing swelling and irritation which causes sneezing, itching and a blocked or runny nose.

How is Mometasone Furoate Suspension used?
Mometasone Furoate 50 micrograms/actuation nasal spray, suspension is sprayed in to the nostrils.

The recommended dose is two sprays into each nostril once a day. The maximum daily dose is four sprays into each nostril once a day.

This medicine can only be obtained with a prescription.

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 Mometasone Furoate Suspension have been shown in studies?
Because Mometasone Furoate Suspension is submitted as a hybrid application, studies in patients have been limited to tests to determine that it is therapeutically equivalent to the reference product, Nasonex 50 micrograms/actuation Nasal Spray, Suspension. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.
What are the possible side effects of Mometasone Furoate Suspension?
The most common side effect with Mometasone Furoate Suspension (which may affect more than 1 in 10 people) is nose bleeds.

The common side effects with Mometasone Furoate Suspension (which may affect up to 1 in 10 people) are headache, sneezing and irritation/burning sensation of the nose, sore nose or throat, ulcers in the nose and respiratory tract infection.

For the full list of all side effects reported with this medicine, see section 4 of the package leaflet or the Summary of Product Characteristics (SmPC) available on the MHRA website.

Why was Mometasone Furoate Suspension approved?
The MHRA decided that the benefits of Mometasone Furoate Suspension 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 Suspension?
A Risk Management Plan has been developed to ensure that Mometasone Furoate Suspension 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 Suspension, 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 Suspension
Germany and the UK agreed to grant a Marketing Authorisation for Mometasone Furoate Suspension on 20 July 2016. A Marketing Authorisation was granted in the UK on 12 August 2016.

The full PAR for Mometasone Furoate Suspension follows this summary.

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

This summary was last updated in September 2016.
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I INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the Reference Member State (RMS) and Concerned Member State (CMS) considered that the application for Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension (UK/H/6175/001/DC; PL 00289/2037), was approvable. The product is a prescription only medicine (POM), indicated for use in adults to treat the symptoms of seasonal allergic rhinitis.

This is a duplicate submission of the previously submitted applications for Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension (PL 00289/1217 & 1748, UK/H/4971 & 5213/001/DC). The application was submitted using the Decentralised Procedure (DCP), with the UK as RMS and Germany as CMS.

The application was made under Article 10(3) of Directive 2001/83/EC, as amended. The reference medicinal product for this application is Nasonex 50 microgram/s actuation Nasal Spray, Suspension, originally granted to Schering-Plough Ltd (PL 00201/0216) on 10 April 1997. The reference licence underwent a change of ownership procedure to the current Marketing Authorisation Holder, Merck Sharp & Dohme Limited (PL 00025/0587), on 14 January 2011.

Mometasone furoate is a topical glucocorticosteroid with local anti-inflammatory properties at doses that are not systemically active.

It is likely that much of the mechanism for the anti-allergic and anti-inflammatory effects of mometasone furoate lies in its ability to inhibit the release of mediators of allergic reactions. Mometasone furoate significantly inhibits the release of leukotrienes from leucocytes of allergic patients.

No new non-clinical studies were conducted, which is acceptable given that this is a hybrid application, which refer to an originator product that has been licensed for over 10 years.

This application is supported by two pivotal bioequivalence studies. The applicant has provided in-vitro characterisation data to support the claim of generic equivalence of the test product to the reference medicinal product, Nasonex 50 micrograms/actuation Nasal Spray, suspension. As a basis for investigation of in-vitro equivalence, reference is made to the EMEA Guideline on the Requirements for Clinical Documentation for Orally Inhaled Products (OIP) including the Requirements for Demonstration of Therapeutic Equivalence between Two Inhaled Products for Use in the Treatment of Asthma and Chronic Obstructive Pulmonary Disease (COPD) in Adults and for Use in the Treatment of Asthma in Children and Adolescents (CPMP/EWP/4151/00 Rev. 1) for the essential requirements to be fulfilled.

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 and assembly of this product.

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.

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

All involved Member States agreed to grant a Marketing Authorisation for the above product at the end of the procedure (Day 210 – 20 July 2016). After a subsequent national phase, the UK granted a
Marketing Authorisation (PL 00289/2037) for this product on 12 August 2016.
II QUALITY ASPECTS

II.1 Introduction
Each actuation (0.1 ml) of the pump delivers a metered dose of 50 micrograms mometasone furoate (as mometasone furoate monohydrate). Other ingredients consist of the pharmaceutical excipients microcrystalline cellulose and carmellose sodium (Avicel RC – 591), glycerol, sodium citrate dehydrate, citric acid monohydrate, polysorbate 80, benzalkonium chloride and water for Injection.

All excipients comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients.

The finished product is packed in a white, high density polyethylene (HDPE) bottle, that contains 10 g (60 actuations) or 18 g (120 or 140 actuations) of product formulation, supplied with a metered-dose, manual polypropylene spray pump and actuator.

Pack sizes are:
10g, 1 bottle containing 60 actuations
18g, 1 bottle containing 120 actuations
18g, 1 bottle containing 140 actuations
Multipack: 2 bottles, each containing 140 actuations (280 actuations in total)
Multipack: 3 bottles, each containing 140 actuations (420 actuations in total)

Specifications and Certificates of Analysis for all packaging materials have been provided. These are satisfactory. All primary packaging complies with relevant EU legislation regarding contact with food.

II.2. Drug Substance

INN: Mometasone furoate monohydrate
Chemical name: 9,21-dichloro-11β-hydroxy-16α-methyl-3,20-dioxopregna-1,4-dien-17-yl-furan-2-carboxylate monohydrate

Structure:

Molecular formula: C_{27}H_{30}Cl_{2}O_{6} \cdot H_{2}O
Molecular weight: 539.4 g/mol
Description: white to almost white powder.
Solubility: It is practically insoluble in water, soluble in acetone, soluble in methylene chloride and slightly soluble in 96% ethanol.

Mometasone furoate monohydrate is the subject of an Active Substance Master File (ASMF).

Synthesis of the drug 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 drug substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Certificates of Analysis for all working standards have been provided.

Batch analyses data are provided and comply with the proposed specification.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging used to store the drug substance. Confirmation has been provided that the primary packaging complies with current guidelines concerning materials in contact with food.

Appropriate stability data have been generated, supporting a suitable retest period when the drug substance is stored in the packaging proposed.

II.3. Medicinal Product

Pharmaceutical Development
The objective of the development programme was to produce a robust formulation of Mometasone Furoate 50 micrograms/actuation Nasal Spray, suspension that will be qualitatively and quantitatively equivalent in composition and also therapeutically equivalent to the reference medicinal product, Nasonex® 50 micrograms/actuation Nasal Spray (Merck Sharp & Dohme Ltd).

Comparative impurity profiles and qualitative composition of the reference and test products have been provided.

Manufacture of the product
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Satisfactory process validation data on 3 full-scale batches of the 140 dose presentation and one full scale batch of the 60 dose presentation have been provided.

Finished Product Specification
The finished product specification is satisfactory. The test methods have been described and adequately validated. Batch data have been provided, which comply with the release specification. Certificates of Analysis have been provided for any 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. The data from these studies support a shelf-life of 2 years (use within 8 weeks of first use) with storage conditions “Do not store above 25°C” and “Do not freeze” are set. These are satisfactory.

II.4 Discussion on chemical, pharmaceutical and biological aspects
There are no objections to the approval of this application from a pharmaceutical viewpoint.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of mometasone furoate monohydrate are well-known, no new non-clinical studies are required and none have been provided. 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**
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

**III.3 Pharmacokinetics**
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

**III.4 Toxicology**
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

**III.5 Ecotoxicity/environmental risk assessment (ERA)**
Since Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension is intended for generic substitution, its use will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

**III.6 Discussion on the non-clinical aspects**
There are no objections to the approval of this application from a non-clinical viewpoint.

**IV CLINICAL ASPECTS**

**IV.1 Introduction**
This formulation was developed to be as similar to the reference, Nasonex® 50 micrograms/actuation Nasal Spray, Suspension, containing the same qualitative and quantitative composition of active and comparable excipients. In order to comply with guidelines EMEA/CHMP/QWP/49313/2005 Corr and CPMP/EWP/4151/00 Rev.1 the applicant has conducted the following studies:

- An investigational pharmacokinetic (PK) study using the reference product, Nasonex. This was designed to characterise the PK profiles of mometasone and to establish the relationship between dose, C\text{max} and AUC in order to decide the optimal dose for definitive PK comparison.
- Two pilot PK studies using 200 micrograms (the most commonly used clinical dose) designed (with and without charcoal), to optimise the design of the pivotal studies, by gauging variability, effect of charcoal etc.
- Two pivotal PK studies (with and without charcoal)

The basis of the bioequivalence studies were considered to be justified since it is reasonable to assume that comparability of plasma levels derived from nasal absorption (confirmed by the use of charcoal blockade in one study) will relate to absorption into the nasal mucosal tissues and hence therapeutic efficacy. It follows that therapeutic equivalence can be assumed on the basis of equivalent absorption from the nasal mucosa. The Summary of Product Characteristics (SmPC) is consistent with that of the innovator’s SmPC.

The applicant’s clinical overview has been written by an appropriately qualified person and is considered acceptable.

**IV.2 Pharmacokinetics**
This application is supported by two pivotal bioequivalence studies and the study reports have been submitted with the dossier. In order to focus on key information only, the exploratory PK and pilot
studies - which were conducted in order to optimise the design of the definitive studies have not been discussed in this report.

**Pivotal pharmacokinetic studies**

**Study 1 (with charcoal blockade)**

*This is an open-label, single-dose, randomized, two-period, two-sequence, two-treatment crossover study to evaluate the comparative bioavailability of Mometasone furoate 50 micrograms/actuation nasal spray, suspension and Nasonex® 50 micrograms/actuation nasal spray, suspension administered with activated charcoal to healthy male and female subjects under fasting conditions.*

**Study 2 (without charcoal blockade)**

*This is an open-label, single-dose, randomized, two-period, two-sequence, two-treatment crossover study to evaluate the comparative bioavailability of Mometasone furoate 50 micrograms /actuation nasal spray, suspension and Nasonex® 50 micrograms /actuation nasal spray, suspension administered to healthy male and female subjects (without activated charcoal) under fasting conditions.*

The role of activated charcoal in study 1 was used to prevent the absorption of mometasone from the gastrointestinal (GI) tract, to ensure that the measured mometasone furoate in the systemic circulation was the result of drug absorbed from the nasal route only.

**Methods**

Based on the pilot study results, the 200 micrograms dose was selected for these pivotal studies for the following reasons:

- The deviation from linearity is very small
- The 200 micrograms dose is situated in the middle of the tested range and, as the data show, allows for detection of even small differences in bioavailability in both positive or negative direction (increase or decrease)
- The 200 micrograms is contained in a manageable volume of suspension that can be accurately dispensed and held by the subjects in their nostrils
- The 200 micrograms is the common dose approved for the major part of the patient's population.

In both studies, after an overnight fast of at least 10 hours, subjects self-administered study drug into each nostril, in accordance with the randomisation schedule. Four actuations (two per nostril) were administered according to product literature recommendations.

In study 1, 10 g (approximately 45 ml) of activated charcoal suspension was administered orally approximately 2 minutes prior to dosing and then at 2, 30, 60, 90,120 and 180 minutes (± 5 minutes) after study drug administration. A 7 day washout-period separated dosing occasions.

Blood samples for plasma mometasone furoate assay were collected during each study period at the following times:

Pre-dose then at 0.167, 0.333, 0.5, 0.667, 0.833, 1.0, 1.25, 1.5, 1.75, 2, 2.25, 2.5, 3, 4, 6, 8, 12, 16, 24, 36 and 48 hours post-dose (and additionally at 72 hours without charcoal study).

The design of the studies is acceptable and the wash-out period and blood sampling schedules were considered adequate. The reference product used is considered to be appropriate.

**Populations studied and sample size-calculation**

In both studies eligible subjects were healthy males aged ≥ 18 years who fulfilled standard entry criteria, in accordance with the protocol.
Study 1 - Charcoal Blockade: Preliminary in-house data indicated a coefficient of variation (CV) for $C_{\text{max}}$ of approximately 45% for mometasone furoate administered with activated charcoal. Assuming a 45% intra-subject variability and a difference between the treatment means of 5% or less, the necessary sample size for a 90% probability of the 90% confidence interval of the treatment means ratio to be within the 80.00–125.00% range was estimated to be 110 subjects. Ten extra subjects were included into the study to account for potential dropouts. Therefore, 120 subjects were enrolled into this study.

Study 2 - Without Charcoal Blockade: Preliminary in-house data indicated a CV for $C_{\text{max}}$ of approximately 25% for mometasone furoate. Assuming a 27.5% intra-subject variability and a difference between the treatment means of 5% or less, the necessary sample size for a 90% probability of the 90% confidence interval of the treatment means ratio to be within the 80.00–125.00% range was estimated to be 44 subjects. Four extra subjects were included into the study to account for potential dropouts. Therefore, 48 subjects were enrolled into this study.

Analytical method
Bioanalysis was carried out and the analytical reports have been submitted. Concentrations of plasma mometasone furoate were determined using a validated Liquid Chromatography Mass Spectrometry (LC-MS/MS) methodology.

For both studies the analytical method is acceptable and adequately validated (pre study and within study) and the handling of samples is adequate. Statements of GLP compliance have been provided.

Statistical methods
Descriptive statistics were calculated for plasma concentrations and for all the pharmacokinetic parameters in each treatment. Analysis of variance (ANOVA) was performed on log-transformed AUC$_t$, AUC$_{\text{inf}}$ and $C_{\text{max}}$ parameters. In the analysis of the combined dataset from all four groups, the significance of the group, sequence-within group, period-within-group, treatment, treatment-by-group interaction and subject-within-sequence-by-group were tested. The least-squares means, the differences between the treatments least-squares means, and the corresponding standard errors of these differences were estimated for log-transformed AUC$_t$, AUC$_{\text{inf}}$ and $C_{\text{max}}$ parameters.

The statistics have been adequately described and the methodology is considered to be acceptable.

Results
Table 1: Summary of the PK results from Study 1 (with charcoal)
Table 2: Summary of the PK results from Study 2 (without charcoal)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Trial</th>
<th>n</th>
<th>Arithmetic Mean (CV%)</th>
<th>Geometric Mean</th>
<th>Ratio(%) A vs B</th>
<th>90% Confidence Interval</th>
<th>Intra-SubjCV(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (pg/mL)</td>
<td>A</td>
<td>48</td>
<td>8.288 (44)</td>
<td>7.693</td>
<td>96.29</td>
<td>86.84 - 106.76</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>48</td>
<td>8.679 (44)</td>
<td>7.990</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC_t (pg h/mL)</td>
<td>A</td>
<td>48</td>
<td>84.037 (40)</td>
<td>78.105</td>
<td>101.46</td>
<td>92.24 - 111.60</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>48</td>
<td>83.463 (41)</td>
<td>76.979</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC_inf (pg h/mL)</td>
<td>A</td>
<td>36</td>
<td>96.295 (36)</td>
<td>88.551</td>
<td>96.33</td>
<td>86.92 - 106.75</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>39</td>
<td>99.077 (39)</td>
<td>91.924</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As can be seen (Tables 1 and 2), for both studies (with and without charcoal blockade) the 90% confidence intervals for the Test/Reference (T/R) mean ratios of ln-transformed pharmacokinetic variables Cmax and AUC0-t in both studies are completely contained within the conventional bioequivalence 90% confidence interval (CI) limits of 80% to 125%. Therefore, the proposed product can be considered bioequivalent to Nasonex® 50 micrograms /actuation nasal spray, suspension under fasting conditions, with and without charcoal blockade. The absorption from the nasal mucosa is, itself, equivalent and hence equivalent absorption and therapeutic effect within the nasal mucosa can be anticipated.

IV.3 Pharmacodynamics
No new pharmacodynamic studies have been conducted, and are not required for these applications since the pharmacodynamic actions of mometasone furoate relevant to the proposed indication are already well characterised.

IV.4 Clinical efficacy
No new efficacy data are presented for this application and none are required.

IV.5 Clinical safety
In terms of safety findings, both the Test and Reference formulations were well tolerated in both bioequivalence studies. In the charcoal study, the most frequently reported adverse event was mild nausea which was reported by 21 subjects (17.5%); 14 on Test and 13 on Reference treatment. No serious adverse events were reported. The most frequently reported adverse event in the study without charcoal was bacteruria which was reported in 5 subjects (10%); 2 on Test formulation and 3 on Reference. The Investigator did not consider these events were related to study treatment.

There are no new safety concerns in relation to mometasone furoate and, in particular, the proposed new generic formulation arising from these studies.

IV.6 Risk Management Plan (RMP) and Pharmacovigilance system
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 50 micrograms/actuation Nasal Spray, Suspension.
<table>
<thead>
<tr>
<th>Safety concern</th>
<th>Routine risk minimisation measures</th>
<th>Additional risk minimisation measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal septum perforation</td>
<td>Warnings in SmPC section 4.4 that mometasone furoate nasal spray is not recommended in case of nasal septum perforation. Listed in SmPC section 4.8 with frequency unknown</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>Growth retardation in children receiving prolonged treatment</td>
<td>Warnings in SmPC section 4.4:</td>
<td>Not applicable.</td>
</tr>
<tr>
<td></td>
<td>• Possibility of systemic effects of nasal corticosteroids, including growth retardation in children and adolescents particularly at high doses prescribed for prolonged periods</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SmPC section 4.8 lists states that systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.</td>
<td></td>
</tr>
<tr>
<td>Ocular events (cataract, glaucoma, intraocular pressure increased, ocular hypertension, choriotreal disorder)</td>
<td>Warnings in section 4.4 of possibility of systemic effects of nasal corticosteroids, particularly at high doses prescribed for prolonged periods, which may include cataract and glaucoma.</td>
<td>Not applicable.</td>
</tr>
<tr>
<td></td>
<td>Listed in SmPC section 4.8 with frequency unknown</td>
<td></td>
</tr>
<tr>
<td>Psychiatric and behavioural events (psychomotor hyperactivity, sleep disorder, anxiety, depression, aggression)</td>
<td>Warning in SmPC section 4.4 states that systemic effects of nasal corticosteroids, particularly at high doses prescribed for prolonged periods, rarely may include a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Listed in section 4.8 that systemic effects may occur, particularly at high doses prescribed for prolonged periods.</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>Hyperglycaemia (blood glucose increased)</td>
<td>None proposed at the moment. This is potential systemic class effect. Risk will be monitored through routine PhV and labelling changes initiated when necessary.</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>Adrenal suppression</td>
<td>Warnings in SmPC section 4.4:</td>
<td>Not applicable.</td>
</tr>
<tr>
<td></td>
<td>• Possibility of adrenal insufficiency after systemic corticosteroid withdrawal in patients who are transferred from long-term administration of systemically active corticosteroids to Mometasone Furoate Nasal Spray.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Possibility of systemic effects of nasal corticosteroids, including adrenal suppression, at high doses prescribed for prolonged periods.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• If there is evidence for higher than recommended doses being used, additional systemic corticosteroid cover should be</td>
<td></td>
</tr>
<tr>
<td>Safety concern</td>
<td>Routine risk minimisation measures</td>
<td>Additional risk minimisation measures</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Hypersensitivity (including anaphylactic reaction)</td>
<td>Considered during periods of stress or elective surgery. SmPC section 4.8 states that systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. SmPC section 4.9 states that excessive doses of corticosteroids may lead to suppression of HPA axis function.</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>Risk of infection when used in immunocompromised patients</td>
<td>In SmPC section 4.3 drug is contraindicated in patients with known hypersensitivity. Listed in SmPC section 4.8 with frequency unknown: Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm, and dyspnoea</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>Use in the presence of other infections (untreated localised infection involving the nasal mucosa, with active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections or ocular herpes simplex)</td>
<td>Contraindication in section 4.3: • Mometasone Furoate Nasal Spray should not be used in the presence of untreated localised infection involving the nasal mucosa. Warning in SmPC section 4.4: • potentially immunosuppressed patients should be warned of the risk of exposure to certain infections (e.g., chickenpox, measles) and of the importance of obtaining medical advice if such exposure occurs.</td>
<td>Not applicable.</td>
</tr>
</tbody>
</table>

Use in the presence of other infections (untreated localised infection involving the nasal mucosa, with active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections or ocular herpes simplex) | Contraindication in section 4.3: • Mometasone Furoate Nasal Spray should not be used in the presence of untreated localised infection involving the nasal mucosa such as herpes simplex Warnings in SmPC section 4.4: • It should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections • If localised fungal infection of the nose or pharynx develops, discontinuation of Mometasone Furoate Nasal Spray therapy or appropriate treatment may be required. Pharyngitis and Upper respiratory tract infection (for... | Not applicable.                      |
### IV.7 Discussion on the clinical aspects

The grant of a Marketing Authorisation is recommended for this application.

### V User consultation

The applicant has provided a bridging report. The proposed leaflet has been bridged to an approved leaflet for Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension (UK/H/4971&5213/001/DC). This is satisfactory.

### VI Overall conclusion, benefit/risk assessment and recommendation

The quality of the product is acceptable, and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with mometasone furoate monohydrate is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
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 approved labelling for Mometasone Furoate 50 micrograms/actuation Nasal Spray, Suspension is presented below:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING CARTON

1. NAME OF THE MEDICINAL PRODUCT

Mometasone Furoate 50 microgram/actuation Nasal Spray, Suspension

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each actuation (0.1 ml) delivers 50 micrograms mometasone furoate (as the monohydrate)
Total weight of one actuation is 100 mg.

3. LIST OF EXCIPIENTS

Excipients
Benzalkonium Chloride
Citric Acid Monohydrate
Glycerol
Microcrystalline Cellulose and Carmellose Sodium
Polysorbate 80
Sodium Citrate Dihydrate
Water for Injection
See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Nasal Spray Suspension

One 10g bottle contains 60 actuations
One 15g bottle contains 120 actuations
One 15g bottle contains 140 actuations
Multipack: 280 (2 bottles of 140) actuations
Multipack: 420 (3 bottles of 140) actuations

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For nasal Use.
Shake gently before use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.
7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not pierce the nasal actuator

8. EXPIRY DATE

EXP: (date to be overprinted)
Use within 8 weeks of first use
Date of opening: (space for user to complete)

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Do not freeze

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

Disposal: please read the package leaflet.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

TEVA UK Limited, Eastbourne, BN22 9AG

12. MARKETING AUTHORISATION NUMBER(S)

PL 00289/2037

13. BATCH NUMBER

BN: (number to be overprinted)

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

For hay fever

16. INFORMATION IN BRAILLE

Mometasone Furoate 50 microgram/actuation Nasal Spray, Suspension
MINIMUM PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING UNITS Label

1. NAME OF THE MEDICINAL PRODUCT

Mometasone Furoate 50 microgram/actuation Nasal Spray, Suspension

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each actuation (0.1 ml) delivers 50 micrograms mometadione furoate (as the monohydrate).

3. LIST OF EXCIPIENTS

Contains benzalkonium chloride
See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Nasal Spray Suspension

60 actuations
120 actuations
140 actuations
Multipack: 280 (2 bottles of 140) actuations
Multipack: 420 (3 bottles of 140) actuations

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For nasal use
Shake gently before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: (date to be overprinted)
Use within 8 weeks of first use
Date of opening (space for user to complete)

9. SPECIAL STORAGE CONDITIONS
Do not store above 25°C. Do not freeze.

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

Disposal: please read the package leaflet.

11. NAME AND ADDRESS OF MARKETING AUTHORISATION HOLDER

TEVA UK Limited, Eastbourne, BN22 9AG

12. MARKETING AUTHORISATION NUMBER

PL 00289/2037

13. BATCH NUMBER

BN: (number to be overprinted)

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

For hay fever

16. INFORMATION IN BRAILLE

Not applicable on labels
# 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)

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