IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Monadia 50mcg/actuation Nasal spray, suspension
Mometasone furoate monohydrate
PA1958/008/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Monadia 50 microgram/actuation Nasal spray from Diapharm GmbH & Co. KG on 10th May 2024 for use in adults and children from 3 years of age and older to treat the symptoms of seasonal allergic rhinitis.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Nasonex 50 micrograms/actuation nasal spray suspension, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Monadia. Monadia has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Nasonex.

Ireland acted as Reference Member State in this decentralised procedure. Germany was a Concerned Member State.

The prescription status of Monadia in Ireland is for supply through pharmacies on prescription which may not be renewed.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie.

Name of the product	Monadia Nasal spray
Name(s) of the active substance(s) (INN)	Mometasone furoate monohydrate
Pharmacotherapeutic classification (ATC code)	R01AD09
Pharmaceutical form and strength(s)	Nasal spray, suspension, 50mcg
Marketing Authorisation Number(s) in Ireland (PA)	PA1958/008/001
Marketing Authorisation Holder	Diapharm GmbH & Co. KG
MRP/DCP No.	IE/H/1261/001/DC
Reference Member State	IE
Concerned Member State	DE

II. QUALITY ASPECTS

II.1. Introduction

This application is for Monadia 50 microgram/actuation Nasal spray, suspension.

II.2 Drug substance

The active substance is mometasone furoate monohydrate, an established active substance described in the European Pharmacopoeia, and is manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

II.3 Medicinal product

P.1 Composition

Each actuation delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 micrograms mometasone furoate.

The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form. Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

P.4 Control of Other Substances (Excipients/*Ancillary Substances*)

Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

P.5 Control of Finished Product

Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

P.6 Packaging material

Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

P.7 Stability of the Finished Product

The proposed shelf life of 35 months (3 years) and an in-use shelf-life of 2 months with 'Do not store above 25°C. Do not freeze.' as storage conditions for the drug product, are in line with the reference product. Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

Reference is made to the up-to-date chemical-pharmaceutical documentation of the original dossier for Nasonex, which has been considered assessed and authorised.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This is an Article 10c of Directive 2001/83/EC (informed consent) application with the reference product being Nasonex 50 micrograms/actuation, nasal spray, suspension, [procedure number: SE/H/1821/001], Organon Pharma (Ireland) Ltd., registered in 1998.

No new preclinical data have been submitted. This is acceptable for this type of application.

III.2 Ecotoxicity/environmental risk assessment

Summary of main study results

Substance (INN/Invented Name): Mometasone			
CAS-number (if available): 141646-00-6			
PBT screening		Result	**Conclusion**
Bioaccumulation potential- log K_{ow}	OECD107	4.66 @ pH 5	Potential PBT (Y)

		4.68 @ pH 7 4.81 @ pH 9	
PBT-assessment			
Parameter	**Result relevant for conclusion**		**Conclusion**
Bioaccumulation	log K_{ow}	4.66 @ pH 5 4.68 @ pH 7 4.81 @ pH 9	
	BCF	136.9-138.3	not B
Persistence	DT50 or ready biodegradability	> 1000 d	vP
Toxicity	NOEC Fish	3.13 ng/L	T
PBT-statement :	The compound is not considered as PBT nor vPvB		
Phase I			
Calculation	**Value**	**Unit**	**Conclusion**
PEC surface water, default	0.004	mg/L	> 0.01 threshold (N)
Other concerns (e.g. chemical class)		Endocrine disruptor	Tailored risk assessment
Phase II Physical-chemical properties and fate			
Study type	**Test protocol**	**Results**	**Remarks**
Adsorption-Desorption	OECD 106	K_{oc} = 5255 mL/g for activated sludge DU Soil K_{oc} = 3640 ml/g MT soil K_{oc} = 9041 ml/g MSL soil K_{oc} = 9179 ml/g OE soil K_{oc} = 4665 ml/g RM soil K_{oc} = 10592 ml/g	Koc sludge < 10,000 L/kg, no risk assessment for terrestrial compartment
Biodegradability Test	OECD 314B	Primary Biodegradation half-life (loss of parent): 31 days	
Aerobic and Anaerobic Transformation in Aquatic Sediment systems	OECD 308	<u>Taunton River system</u> $DT_{50, water, 20 °C}$ = 3.7 days $DT_{50, sediment, 20 °C}$ = >1000 days $DT_{50, whole system, 20 °C}$ = >1000 days <u>Weweantic River system</u> $DT_{50, water, 20 °C}$ = 4.2 days	

		$DT_{50, sediment, 20 °C}$ = >1000 days $DT_{50, whole system, 20 °C}$ = 512 days			
Phase IIa Effect studies					
Study type	**Test protocol**	**Endpoint**	**value**	**Unit**	**Remarks**
Algae, Growth Inhibition Test/ *Pseudokirchneriella subcapitata*	OECD 201	NOEC	3.2	mg/L	
Daphnia sp. Reproduction Test	OECD 211	NOEC	0.34	mg/L	
Fish, Early Life Stage Toxicity Test/ *Pimephales promelas*	OECD 210	NOEC	0.14	µg/L	
Fish, sexual development study/*Danio rerio*	OECD 234	NOEC	3.13	ng/L	Sex ratio Risk to surface water
Activated Sludge, Respiration Inhibition Test	OECD 209	EC_{15}	>1000	mg/L	
Phase IIb Studies					
Bioaccumulation	OECD 305	BCF	136.9-138.3	L/kg	%lipids: 5 %
Sediment dwelling organism	OECD 218	NOEC	80 (emergence) 10 (development)	mg/kg	*Chironomus riparius*

Conclusions on studies:

Considering the above data, mometasone furoate monohydrate should be used according to the precautions stated in the SmPC in order to minimise any potential risks to the environment.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of mometasone furoate monohydrate are well known. Based on the legal basis of this application, the nonclinical package is considered acceptable.

IV. CLINICAL ASPECTS

IV.1 Introduction

Mometasone furoate monohydrate is a well-known active substance with an established efficacy and safety profile. This medicinal product is the same as Nasonex 50 microgram/actuation Nasal spray, suspension on the European market.

The content of the SmPC approved during the decentralised procedure is closely aligned with that accepted for the reference product Nasonex marketed by Organon Pharma (Ireland) Ltd. However, only the indication for use in adults and children from

3 years of age and older to treat the symptoms of seasonal allergic rhinitis is proposed and is acceptable for an informed consent application.

IV.2 Pharmacokinetics

Absorption
Mometasone furoate, administered as an aqueous nasal spray, has a systemic bioavailability of <1% in plasma, using a sensitive assay with a lower quantitation limit of 0.25 pg/ml.

Distribution
Not applicable as mometasone is poorly absorbed via the nasal route.

Biotransformation
The small amount that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism.

Elimination
Absorbed mometasone furoate is extensively metabolized and the metabolites are excreted in urine and bile.

IV.3 Pharmacodynamics

Pharmacotherapeutic group: Decongestants and Other Nasal Preparations for Topical Use-Corticosteroids
ATC code: R01A D09

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

IV.4 Clinical Efficacy
As this is an informed consent application no new clinical efficacy data has been submitted. Efficacy is expected to be similar to the reference product Nasonex 50 micrograms/actuation, nasal spray.

IV.5 Clinical Safety
As this is an informed consent application no new clinical safety data has been submitted. Safety is expected to be similar to the reference medicinal product Nasonex 50 micrograms/actuation, nasal spray. The safety information in the SmPC and Package Leaflet are in line with those of the reference medicinal product.

A Risk Management Plan, version 1.1, dated 23 June 2023 has been submitted, 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 monohydrate. It is concluded that routine pharmacovigilance and risk minimisation measures are sufficient.

PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

IV.6 Discussion on the clinical aspects

Mometasone furoate monohydrate is a well-known active substance and has been widely marketed.

Monadia 50 microgram/actuation Nasal spray, suspension is an Informed Consent form of Nasonex 50 micrograms/actuation, nasal spray, suspension, which is a well-known medicinal product approved in Europe for the treatment of seasonal allergic rhinitis in adults and children from 3 years of age, which has a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Monadia 50 microgram/actuation Nasal spray, suspension is a prescription-only medicinal product in Ireland.

The content of the SmPC approved during this decentralised procedure is closely aligned with the reference product Nasonex 50 micrograms/actuation, nasal spray, suspension, except that it is amended for use only in adults and children from 3 years of age and older to treat the symptoms of seasonal allergic rhinitis, which is acceptable for an informed consent application.

V. OVERALL CONCLUSIONS

The active substance, mometasone furoate monohydrate, is a well-known active substance with a proven chemical-pharmaceutical quality and an established efficacy and safety profile.

This decentralised application for a marketing authorisation for Monadia 50 microgram/actuation Nasal spray, suspension was submitted to HPRA in accordance with Article 10(c) of Directive 2001/83/EC.

The SmPC is consistent with that of the reference product.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

Monadia 50 microgram/actuation Nasal spray, suspension is the same as Nasonex 50 microgram/actuation Nasal spray, suspension. Nasonex is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

The HPRA, on the basis of the data submitted considered that Monadia 50 microgram/actuation Nasal spray, suspension was the same as the reference product and therefore granted a marketing authorisation.

Following MRP/DCP procedure:
N/A

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
New DCP as RMS	IE/H/1261/001/DC	SmPC, PAR	10th May 2024	9th May 2029