# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Mometasone furoate/Olopatadine Glenmark
25 micrograms/actuation+600 micrograms/actuation
Nasal Spray, suspension

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One delivered dose (the dose that leaves the actuator) contains mometasone furoate monohydrate equivalent to 25 microgram mometasone furoate and olopatadine hydrochloride equivalent to 600 micrograms olopatadine.

Excipient with known effect
Each actuation contains 0.02 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Nasal Spray, Suspension.
White, homogeneous suspension.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

[Invented name] is indicated in adults and adolescents 12 years of age and older for the treatment of moderate to severe nasal symptoms associated with allergic rhinitis.

### 4.2 Posology and method of administration

**Posology**

Adults and adolescents (12 years and older)
The usual recommended dose is two actuations in each nostril twice daily (morning and evening).

Children below 12 years
[Invented name] is not recommended for use in children below 12 years of age as safety and efficacy has not been established in this age group.

Elderly
No dose adjustment is required in this population.

Renal and hepatic impairment
There are no data in patients with renal and hepatic impairment, however no dose adjustment is expected to be required in these populations considering the absorption, metabolism and elimination of the active substances (see section 5.2).

**Method of administration**

[Invented name] is for nasal use only.

Prior to administration of the first dose, shake container well and actuate the pump 6 times (until a uniform spray is obtained). If the pump is not used for 14 days or longer, re-prime the pump with 2 actuations until a uniform spray is observed, before next use.

Shake container for minimum 10 seconds before each use. After using the spray, wipe the nozzle carefully with a clean handkerchief or tissue and replace the cap, to avoid that the nozzle gets blocked. The bottle should be discarded after the labelled number of actuations or within 2 months of first use.

## 4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

[Invented name] should not be used in the presence of untreated localised infection involving the nasal mucosa, such as herpes simplex.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal surgery or trauma should not use a nasal corticosteroid until healing has occurred.

## 4.4 Special warnings and precautions for use

Local Nasal Effects
Instances of nasal ulceration and nasal septal perforation have been reported in patients following the intranasal application of antihistamines.
Instances of nasal septal perforation have been reported following the intranasal application of corticosteroids.
Patients using [Invented name] over several months or longer should be examined periodically for possible changes in the nasal mucosa.
[Invented name] is not recommended in case of nasal septum perforation (see section 4.8).

Instances of epistaxis have been reported in patients following the intranasal application of antihistamines and corticosteroids (see section 4.8).

In clinical studies with mometasone furoate administered intranasally, the development of localised infections of the nose and pharynx with *Candida albicans* has occurred. When such an infection develops, it may require treatment with appropriate local therapy and discontinuation of treatment with [Invented name]. Patients using [Invented name] over several months or longer should be examined periodically for evidence of Candida infection or other signs of adverse effects on the nasal mucosa.

Visual disturbances
Visual disturbance may be reported with systemic and topical (including, intranasal) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Hypersensitivity Reactions
Hypersensitivity reactions, including instances of wheezing, may occur after the intranasal administration of mometasone furoate monohydrate and olopatadine hydrochloride. Discontinue [Invented name] if such reactions occur (see section 4.8).

Immunosuppression
Persons who are using drugs that suppress the immune system, such as corticosteroids, are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible children or adults using corticosteroids. In children or adults who have not had these diseases or been properly immunized, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known.

Corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract, untreated local or systemic fungal or bacterial infections, systemic viral or parasitic infections, or ocular herpes simplex because of the potential for worsening of these infections.

Systemic Effects of Corticosteroids
Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

When intranasal steroids are used at higher-than-recommended dosages or in susceptible individuals at recommended dosages, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of [Invented name] should be discontinued slowly, consistent with accepted procedures for discontinuing oral corticosteroid therapy. The concomitant use of intranasal corticosteroids with other inhaled corticosteroids could increase the risk of signs or symptoms of hypercorticism and/or suppression of the HPA axis.
If there is evidence for higher than recommended doses being used, then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency, and some patients may experience symptoms of withdrawal (e.g., joint and/or muscular pain, lassitude, and depression). Patients previously treated for prolonged periods with systemic corticosteroids and transferred to topical corticosteroids should be carefully monitored for acute adrenal insufficiency in response to stress. In those patients who have asthma or other clinical conditions requiring long-term systemic corticosteroid treatment, too rapid a decrease in systemic corticosteroids may cause a severe exacerbation of their symptoms.

Somnolence
Like other antihistamines, olopatadine may cause somnolence in same patients when absorbed systemically.
Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness and motor coordination, such as operating machinery or driving a motor vehicle, after administration of [Invented name]. Concurrent use of [Invented name] with alcohol or other central nervous system (CNS) depressants should be avoided because additional reductions in alertness and additional impairment of CNS performance may occur.
Somnolence has been reported following administration of [Invented name] in clinical studies (see section 4.8).

Antihistamine effects
Concomitant use of olopatadine (e.g. eyes drops) or other antihistaminic drugs administered via nasal, ocular or oral route may increase the risk of antihistamine adverse effects.

Paediatric population
It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the

dose of nasal corticosteroid if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.

Excipients:
[Invented name] contains 0.02 mg benzalkonium chloride in each actuation. Benzalkonium chloride may cause irritation or swelling inside the nose, especially if used for a long time.

## 4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with [Invented name].
Any drug drug interactions from the combination of olopatadine and mometasone furoate are expected to reflect those of the components taken individually, as no pharmacokinetic interaction between olopatadine and mometasone furoate was observed when administered in combination.

*Olopatadine:*
No interactions between olopatadine and other drugs are expected (see section 5.2).

*Mometasone Furoate*:
Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

## 4.6 Fertility, pregnancy and lactation

Pregnancy
*Mometasone Furoate:*
There are no or limited amount of data from the use of mometasone furoate in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3).

*Olopatadine:*
There are no or limited amount of data from the use of intranasal olopatadine in pregnant women. Studies in animals have shown reproductive toxicity following systemic administration (see section 5.3).

[Invented name] should not be used in pregnancy unless the potential benefit to the mother justifies any potential risk to the mother, foetus or infant. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for hypoadrenalism.

Breast-feeding
*Mometasone Furoate:*
It is unknown whether mometasone furoate is excreted in human milk

*Olopatadine:*
Available data in animals have shown excretion of olopatadine in milk following oral administration (for details see section 5.3). A risk to the newborn/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from [Invented name] therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility
There are only limited data with regard to fertility.
There are no clinical data concerning the effect of mometasone furoate on fertility. Animal studies have shown reproductive toxicity, but no effects on fertility.
There are no clinical data concerning the effect of olopatadine on fertility.

## 4.7 Effects on ability to drive and use machines

In isolated cases dizziness, lethargy, fatigue and somnolence may occur when using [Invented name]. In these cases, the ability to drive and use machines may be impaired. Alcohol may enhance this effect.

## 4.8 Undesirable effects

Summary of the safety profile
The most commonly reported adverse reaction during treatment with [Invented name] was dysgeusia (a substance-specific unpleasant taste), epistaxis and nasal discomfort.

Tabulated list of adverse reactions
The following adverse reactions have been reported during clinical studies and post-marketing data and are classified according to the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) or not known (cannot be estimated from the available data).

| **Frequency**<br>**System Organ Class** | **Common** | **Uncommon** | **Rare** | **Not known** |
|---|---|---|---|---|
| Infection and infestations | | | Bacterial vaginosis | Pharyngitis*<br>Upper respiratory tract infection* |
| Immune system disorders | | | | Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm, and dyspnoea* |
| Psychiatric disorders | | | Anxiety<br>Depression<br>Insomnia | |
| Nervous system disorder | Dysgeusia (unpleasant taste) | Dizziness<br>Headaches<br>Somnolence | Lethargy<br>Migraine | |
| Eye disorders | | | Blurred vision<br>Dry eye<br>Eye discomfort | Cataracts*<br>Glaucoma*<br>Increased intraocular pressure* |
| Ear and labyrinth disorder | | | Ear pain | |
| Respiratory, thoracic and mediastinal disorders | Epistaxis<br>Nasal discomfort | Nasal dryness | Nasal inflammation<br>Nasal mucosal disorder | Nasal septum perforation* |

| | | | | |
|---|---|---|---|---|
| | | | Oropharyngeal pain<br>Sneezing<br>Throat irritation | |
| Gastrointestinal disorders | | Dry mouth<br>Abdominal pain<br>Nausea | Constipation<br>Sore tongue | |
| General disorders and administration site conditions | | Fatigue | | |
| Injury, poisoning and procedural complications | | | Laceration | |

*reported with the use of corticosteroids.

Systemic effects of some nasal corticosteroids may occur, particularly when administered at high doses for prolonged periods (see section 4.4).

Growth retardation has been reported in children receiving nasal corticosteroids. Growth retardation may be possible in adolescents, too (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.*

### 4.9 Overdose

With the nasal route of administration overdose reactions are not anticipated.
No data are available in humans regarding overdose by accidental or deliberate ingestion.
Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of HPA axis function.
There is no known specific antidotes to [Invented name] active components.
In the case of overdose, appropriate monitoring and supportive management of the patient should be implemented.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use, corticosteroids / mometasone, combinations, ATC code: R01AD59

Mechanism of action and pharmacodynamic effects

[Invented name] contains olopatadine hydrochloride and mometasone furoate, which have different modes of action and show synergistic effects in terms of improvement of allergic rhinitis symptoms.

Olopatadine is a potent selective antiallergic/antihistaminic agent that exerts its effects through multiple distinct mechanisms of action. It antagonises histamine (the primary mediator of allergic response in humans).

Mometasone furoate is a topical glucocorticosteroid with local anti-inflammatory properties. 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. In cell culture, mometasone furoate demonstrated high potency in inhibition of synthesis and release of IL-1, IL-5, IL-6 and TNFα; it is also a potent inhibitor of leukotriene production. In addition, it is an extremely potent inhibitor of the production of the Th2 cytokines, IL-4 and IL-5, from human CD4+ T-cells.

Clinical efficacy and safety

In 2 clinical studies (GSP 301-301 and GSP 301-304) in adults and adolescents 12 years of age or older with allergic rhinitis, [Invented name] two sprays in each nostril twice daily improved nasal symptoms (comprising rhinorrhoea, nasal congestion, sneezing and nasal itching) compared with placebo, olopatadine hydrochloride alone and mometasone furoate alone. The results of the two clinical studies are summarised in the Table 1 and Table 2 below.

**Table 1: Mean Change from Baseline in Reflective Total Nasal Symptom Scores Over 2 Weeks* in Adults and Adolescents Aged ≥ 12 Years with Seasonal Allergic Rhinitis in Study GSP 301-301 (full analysis set)**

| | | **Baseline** | **Change From Baseline** | **[Invented name] Treatment Effect Difference** | | |
|---|---|---|---|---|---|---|
| Treatment (2 sprays/nostril twice daily) | N | Mean | LS Mean | LS Mean | 95% CI | P-value† |
| [Invented name] | 299 | 10.1 | -3.48 | -- | -- | -- |
| Placebo | 283 | 10.2 | -2.50 | -0.98 | (-1.38, -0.57) | <0.0001 |
| Olopatadine HCl | 294 | 10.3 | -2.87 | -0.61 | (-1.01, -0.21) | 0.0029 |
| Mometasone furoate | 294 | 10.2 | -3.09 | -0.39 | (-0.79, 0.01) | 0.0587 |

| | | **Baseline** | **Change From Baseline** | **[Invented name] Treatment Effect Difference** | | |
|---|---|---|---|---|---|---|
| Treatment (2 sprays/nostril twice daily) | N | Mean | LS Mean | LS Mean | 95% CI | P-value† |
| [Invented name] | 291 | 10.09 | -3.52 | -- | -- | -- |
| Placebo | 290 | 10.32 | -2.44 | -1.09 | (-1.49, -0.69) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Olopatadine HCl | 290 | 10.16 | -3.08 | -0.44 | (-0.84, -0.05) | 0.028 |
| Mometasone furoate | 293 | 10.20 | -3.05 | -0.47 | (-0.86, -0.08) | 0.019 |

**Table 2: Mean Change from Baseline in Reflective Total Nasal Symptom Scores Over 2 Weeks* in Adults and Adolescents Aged ≥ 12 Years with Seasonal Allergic Rhinitis in Study GSP 301-304 (full analysis set)**

* Average of AM and PM rTNSS for each day (maximum score = 12) and averaged over the 2-week treatment period.
† P-values are nominal
CI= confidence interval; LS= least square;

## 5.2 Pharmacokinetic properties

Absorption
After repeated intranasal administration of 2 sprays per nostril of [Invented name] (2400 microgram of olopatadine and 100 microgram of mometasone furoate) twice daily in patients with seasonal allergic rhinitis, the mean (± standard deviation) peak plasma exposure (Cmax) was 19.80 ± 7.01 ng/mL for olopatadine and 9.92 ± 3.74 pg/mL for mometasone furoate, and the mean exposure over the dosing regimen (AUCtau) was 88.77 ± 23.87 ng*hr/mL for olopatadine and 58.40 ± 27.00 pg*hr/mL for mometasone furoate. The median time to peak exposure from a single dose was 1 hour for both olopatadine and mometasone furoate.

There was no evidence of pharmacokinetic interactions between mometasone furoate and olopatadine hydrochloride.

Distribution
The protein binding of olopatadine was reported as moderate at approximately 55% in human serum and independent of drug concentration over the range of 0.1 to 1000 ng/mL. Olopatadine binds predominately to human serum albumin.

The in vitro protein binding for mometasone furoate was reported to be 98% to 99% in concentration range of 5 to 500 ng/mL.

Biotransformation
The small amount of mometasone furoate that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism.
Olopatadine is not extensively metabolised. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.
In vitro studies have shown that olopatadine did not inhibit metabolic reactions which involve cytochrome P-450 isozymes 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4. These results indicate that olopatadine is unlikely to result in metabolic interactions with other concomitantly administered active substances.

Elimination
Absorbed mometasone furoate is extensively metabolized and the metabolites are excreted in urine and bile. After nasal administration, the half-life of mometasone furoate in plasma was approximately 18 to 20 hours, in healthy volunteers.

From oral pharmacokinetic studies, the half-life of olopatadine in plasma was approximately eight to 12 hours, and elimination was predominantly through renal excretion. Approximately 60-70% of the dose was recovered in the urine as active substance.
After nasal administration, the half-life of olopatadine in plasma was approximately six to seven hours, in healthy volunteers.

Hepatic impairment
*Olopatadine:*
No clinically relevant effect of hepatic impairment is expected on the Olopatadine pharmacokinetics since it is predominantly excreted unchanged via urine (see section 4.2).

*Mometasone furoate:*
A study performed with inhaled mometasone furoate in adults with mild, moderate and severe hepatic impairment has shown that peak plasma concentrations of mometasone furoate appear to increase with severity of hepatic impairment, however, the number of detectable levels were few (see section 4.2).

Renal impairment
*Olopatadine:*
Since olopatadine is excreted in urine primarily as unchanged active substance, impairment of renal function alters the pharmacokinetics of olopatadine with 8-fold greater plasma $AUC_{0-\infty}$ in patients with severe renal impairment (mean creatinine clearance of 13.0 ml/min) compared to healthy adults. Following a 10 mg oral dose in patients undergoing haemodialysis (with no urinary output), plasma olopatadine concentrations were significantly lower on the haemodialysis day than on the non-haemodialysis day suggesting olopatadine can be removed by haemodialysis.

*Mometasone furoate:*
Due to the very low contribution of the urinary pathway to total body elimination of mometasone furoate, the effects of renal impairment on pharmacokinetics of mometasone furoate have not been investigated (see section 4.2).

*Elderly*
Studies comparing the pharmacokinetics of 10 mg oral doses of olopatadine in young (mean age 21 years) and elderly (mean age 74 years) showed no significant differences in the plasma concentrations (AUC), protein binding or urinary excretion of unchanged parent drug and metabolites.

## 5.3 Preclinical safety data

*Olopatadine:*
Non-clinical data reveal no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

Studies in animals have shown reduced growth of nursing pups of dams receiving systemic doses of olopatadine well in excess of the maximum level recommended for human intranasal use. Olopatadine has been detected in the milk of nursing rats following oral administration.

*Mometasone Furoate*:
No toxicological effects unique to mometasone furoate exposure were demonstrated. All observed effects are typical of this class of compounds and are related to exaggerated pharmacologic effects of glucocorticoids.

Preclinical studies demonstrate that mometasone furoate is devoid of androgenic, antiandrogenic, estrogenic or antiestrogenic activity but, like other glucocorticoids, it exhibits some antiuterotrophic activity and delays vaginal opening in animal models at high oral doses of 56 mg/kg/day and 280 mg/kg/day.

Like other glucocorticoids, mometasone furoate showed a clastogenic potential in-vitro at high concentrations. However, no mutagenic effects can be expected at therapeutically relevant doses.

In studies of reproductive function, subcutaneous mometasone furoate, at 15 micrograms/kg prolonged gestation and prolonged and difficult labour occurred with a reduction in offspring survival and body weight or body weight gain. There was no effect on fertility.

Like other glucocorticoids, mometasone furoate is a teratogen in rodents and rabbits. Effects noted were umbilical hernia in rats, cleft palate in mice and gallbladder agenesis, umbilical hernia, and flexed front paws in rabbits. There were also reductions in maternal body weight gains, effects on foetal growth (lower foetal body weight and/or delayed ossification) in rats, rabbits and mice, and reduced offspring survival in mice.

The carcinogenicity potential of inhaled mometasone furoate (aerosol with CFC propellant and surfactant) at concentrations of 0.25 to 2.0 micrograms/l was investigated in 24-month studies in mice and rats. Typical glucocorticoid-related effects, including several non-neoplastic lesions, were observed. No statistically significant dose-response relationship was detected for any of the tumour types.

*[Invented name] Nasal Spray*
Repeated dose intranasal toxicity study in rats for a period up to 13 weeks with [Invented name] revealed no new adverse effects in comparison to the individual components.

Environmental risk assessment (ERA)
Environmental risk assessment studies have shown that mometasone furoate may pose a risk to the aquatic environment (See also Section 6.6)

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Microcrystalline cellulose (E460)
Dibasic sodium phosphate heptahydrate (E 339)
Carmellose sodium (E 466)
Sodium chloride
Benzalkonium chloride
Disodium edetate
Polysorbate 80 (E 433)
Hydrochloric acid (E 507)
Sodium hydroxide (E 524)
Water for injections

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

3 years
In-use shelf life (after first use): 2 months

### 6.4 Special precautions for storage

Do not freeze.

### 6.5 Nature and contents of container

The nasal spray is contained in a white, high density polyethylene bottle supplied with a metered-dose, manual polypropylene spray pump actuator. The actuator is fitted with a HDPE purple cap.

Pack sizes:
1 bottle of 20 ml with 56 actuations,
1 bottle of 20 ml with 120 actuations,
1 bottle of 30 ml with 240 actuations.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

This medicinal product may pose a risk to the environment (See section 5.3).
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

{to be completed nationally}

## 8. MARKETING AUTHORISATION NUMBER(S)

{to be completed nationally}

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

{to be completed nationally}

## 10. DATE OF REVISION OF THE TEXT

29 October 2024