SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MOMATE AZ (Mometasone Furoate and Azelastine Hydrochloride Nasal Spray (50 + 140mcg))

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each spray delivers:
Mometasone Furoate BP ....50 mcg
Azelastine Hydrochloride BP..... 140 mcg
Preservative:
Benzalkonium Chloride BP...0.02% w/w

For full list of excipients, refer to section 6.1.

3. PHARMACEUTICAL FORM

Nasal Spray, Suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Mometasone Furoate and Azelastine Hydrochloride Nasal Spray is indicated for the relief of the symptoms of seasonal allergic rhinitis in patients 12 years of age and older.

4.2 Posology and Method of Administration

Posology

Adult and adolescent patient of 12 years or more:
The recommended dose is one spray in each nostril twice daily.

Paediatric population
Mometasone Furoate and Azelastine Hydrochloride Nasal Spray is not recommended for use in children below 12 years of age as safety and efficacy has not been established in this age group.

Patients with renal impairment
No dose adjustment is needed in patients with mild renal impairment (creatinine clearance
>79 ml/min). For patients with moderate to severe renal impairment (creatinine clearance
< 79 ml/min - >10ml/min), this product is to be used with caution and under strict medical supervision.

Patients with hepatic impairment
No dose adjustment is needed in patients with hepatic impairment.

Method of administration
Mometasone Furoate and Azelastine Hydrochloride Nasal Spray is for nasal use only.

Instruction for use
1. Remove the plastic cap

(Figure 1)

2. Before you use Mometasone Furoate and Azelastine Hydrochloride Nasal Spray for the first time prime the pump by pressing downward on the shoulders of the white nasal applicator using your index finger and middle finger while holding the base of the bottle with your thumb (Figure 2). Do not pierce the nasal applicator. Press down and release the pump 06 times or until a fine spray appears. Do not spray into eyes. The pump is now ready to use. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by spraying 2 times or until a fine spray appears.

(Figure 2)
3. Gently blow your nose to clear the nostrils. Close 1 nostril. Tilt your head forward slightly, keep the bottle upright, carefully insert the nasal applicator into the other nostril (Figure 3). Do not spray directly onto the nasal septum (the wall between the two nostrils.)

4. Then breathe out through the mouth.
5. Repeat in the other nostril.
6. Wipe the nasal applicator with a clean tissue and replace the plastic cap (Figure 4).

(Figure 4)

Patient instruction for cleaning applicator

1. To clean the nasal applicator, remove the plastic cap (Figure 5).

(Figure 5)

2. Pull gently upward on the white nasal applicator to remove (Figure 6).

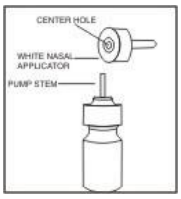
(Figure 6)

3. Soak the Nozzle and Dust Cap in warm water for few minutes and then rinse thoroughly spray tip and dust cap in warm water and finally rinse under clean running water. Repeat the procedure if the mist is not coming out.

(Figure 7)

Note:
Incase during usage for the first time if the actuator is observed to be blocked condition due to accidental pressing during transit or during handling which prompts release of miniscule contents, never use a pin or any sharp objects to pierce to unblock the nozzle instead subject the actuator for cleaning.

4. Put the nasal applicator back together making sure the pump stem is reinserted into the applicator's center hole (Figure 8).



(Figure 8)

5. Reprime the pump by pressing downward on the shoulders of the white nasal applicator using your index and middle fingers while holding the base of the bottle with your thumb. Press down and release the pump 2 times or until a fine spray appears. Do not spray into eyes. The pump is now ready to use. The pump may be stored unused for upto 1 week without repriming. If unused for more than 1 week, reprime by spraying 2 times or until a fine spray appears (Figure 9).

(Figure 9)

6. Replace the plastic cap (Figure 10).

(Figure 10)

4.3 Contraindications

- Hypersensitivity to mometasone furoate, or azelastine hydrochloride, or to any of the excipients listed in section 6.1.
- Nasal Spray 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

Mometasone Furoate

Immunosuppression

Mometasone Furoate Nasal Spray 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, or systemic viral infections.Patients receiving corticosteroids who are potentially immunosuppressed 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.

Local Nasal Effects

Following 12 months of treatment with mometasone furoate nasal spray in a study of patients with perennial rhinitis, there was no evidence of atrophy of the nasal mucosa; also, mometasone furoate tended to reverse the nasal mucosa closer to a normal histologic phenotype. Nevertheless, patients using mometasone furoate nasal spray over several months or longer should be examined periodically for possible changes in the nasal mucosa. If localised fungal infection of the nose or pharynx develops, discontinuance of mometasone furoate nasal spray therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuing mometasone furoate nasal spray.

Mometasone furoate nasal spray is not recommended in case of nasal septum perforation.

In clinical studies, epistaxis occurred at a higher incidence compared to placebo. Epistaxis was generally self-limiting and mild in severity.

Systemic Effects of Corticosteroids

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. 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).

Following the use of intranasal corticosteroids, instances of increased intraocular pressure have been reported.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) 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.

Patients who are transferred from long-term administration of systemically active corticosteroids to intranasal mometasone require careful attention. Systemic corticosteroid withdrawal in such patients may result in adrenal insufficiency for a number of months until recovery of HPA axis function. If these patients exhibit signs and symptoms of adrenal insufficiency or symptoms of withdrawal (e.g., joint and/or muscular pain, lassitude, and depression initially) despite relief from nasal symptoms, systemic corticosteroid administration should be resumed and other modes of therapy and appropriate measures instituted. Such transfer may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

Treatment with higher than recommended doses may result in clinically significant adrenal suppression. 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.

Nasal Polyps

The safety and efficacy of intranasal mometasone has not been studied for use in the treatment of unilateral polyps, polyps associated with cystic fibrosis, or polyps that completely obstruct the nasal cavities.

Unilateral polyps that are unusual or irregular in appearance, especially if ulcerating or bleeding, should be further evaluated.

Effect on Growth in 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.

Non-nasal Symptoms

Although intranasal mometasone will control the nasal symptoms in most patients, the concomitant use of appropriate additional therapy may provide additional relief of other symptoms, particularly ocular symptoms.

Azelastine Hydrochloride

None.

Mometasone Furoate and Azelastine Hydrochloride Nasal Spray contains benzalkonium chloride. 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 specific drug-drug interaction studies have been performed with the fixed dose combination of Mometasone Furoate and Azelastine Hydrochloride Nasal Spray. The data are complied with the available information from the individual components of the fixed dose combination. Also since both Mometasone and Azelastine metabolizes with different receptors, there are no drug-drug interaction anticipated with the use of this fixed dose combination.

Mometasone Furoate

A clinical interaction study was conducted with loratadine. No interactions were observed.

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.

Azelastine Hydrochloride

No specific interactions have been studied.

4.6 Fertility, Pregnancy and lactation

No specific studies have been performed with fixed dose combination of Mometasone Furoate and Azelastine Hydrochloride Nasal Spray on pregnant and lactating females.

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. As with other nasal corticosteroid preparations, mometasone furoate nasal spray 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.

Azelastine Hydrochloride

At high oral doses in animals, 500 times the proposed oral human daily dose, foetal death, growth retardation and an increased incidence of skeletal abnormalities occurred during reproduction toxicity testing. Due to the nasal route of administration and the low dose administered, minimal

systemic exposure can be expected. However as with all medicines caution should be exercised with use during pregnancy.

Lactation

Mometasone Furoate

It is unknown whether mometasone furoate is excreted in human milk. As with other nasal corticosteroid preparations, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from intranasal mometasone therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Azelastine Hydrochloride

Due to the nasal route of administration and the low dose administered, minimal systemic exposure can be expected. However as with all medicines caution should be exercised with use during lactation.

Fertility

Mometasone Furoate

There are no clinical data concerning the effect of mometasone furoate on fertility. Animal studies have shown reproductive toxicity, but no effects on fertility.

Azelastine Hydrochloride

None.

4.7 Effects on ability to drive and use machines

No studies on the effect of fixed dose combination of Mometasone Furoate and Azelastine Hydrochloride Nasal Spray on the ability to drive or use machines have been performed. In the pivotal efficacy study conducted, this fixed dose combination did not show any adverse event like dizziness or impairment of mental alertness. Therefore, patients intending to drive, engage in potentially hazardous activities or operate machinery should take their response to the medicinal product into account.

Mometasone Furoate

There is no known information on the effect of Mometasone Furoate on the ability to drive or use machinery. However, vision blurred may experience with mometasone furoate nasal spray.

Azelastine Hydrochloride

Azelastine Hydrochloride has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following listing of undesirable effects is based on data from a clinical trial (560 patients) and from post-marketing surveillance study of individual components of the FDC with reporting rates classified as adverse reactions are ranked under heading of frequency, using 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 <1/1,000)
- Very rare (<1/10,000) including isolated cases

Mometasone Furoate and Azelastine Hydrochloride Nasal Spray

In a clinical study conducted in 560 patients with seasonal allergic rhinitis, 282 patients were exposed to Mometasone Furoate and Azelastine Hydrochloride Nasal Spray for a mean duration of 14.94 days.

Overall, the safety profile of Mometasone Furoate and Azelastine Hydrochloride Nasal Spray was comparable to individual monotherapies treatment in the study, and was also consistent with the published literature for individual monotherapy available. A total of 18 adverse events related to the combination of Mometasone Furoate and Azelastine Hydrochloride Nasal Spray were reported in 11/282 patients. Most common adverse reactions reported in study were headache (5 cases) and dysgeusia (5 cases). The other adverse reactions were somnolence (3 cases), lethargy (2 cases), nausea (1 case), dyspepsia (1 case) and sneezing (1 case). Most of the adverse events were mild in severity and there were no severe adverse events reported during the study.

Below is the adverse drug reactions reported with the individual components of the fixed dose combination.

Mometasone Furoate

Summary of the safety profile

Epistaxis was generally self-limiting and mild in severity, and occurred at a higher incidence compared to placebo (5%), but at a comparable or lower incidence when compared to the active control nasal corticosteroids studied (up to 15%) as reported in clinical studies for allergic rhinitis. The incidence of all other adverse events was comparable with that of placebo. In patients treated for nasal polyposis, the overall incidence of adverse events was similar to that observed for patients with allergic rhinitis.

Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

Tabulated list of adverse reactions

Treatment related adverse reactions (≥1%) reported in clinical trials in patients with allergic rhinitis or nasal polyposis and post-marketing regardless of indication are presented in Table 1. Adverse reactions are listed according to MedDRA primary system organ class. Within each system organ class, adverse reactions are ranked by frequency. Frequencies were defined as follows: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100). The frequency of post-marketing adverse events are considered as "not known (cannot be estimated from the available data)".

Table 1: Treatment-related adverse reactions reported by system organ class and frequency

	Very common	Common	Not known
Infections and infestations		Pharyngitis Upper respiratory tract infection†	
Immune system disorders			Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm and dyspnea
Nervous system disorders		Headache	
Eye disorders			Glaucoma Increased intraocular pressure Cataracts Vision blurred
Respiratory, thoracic and mediastinal disorders	Epistaxis*	Epistaxis Nasal burning Nasal irritation Nasal ulceration	Nasal septum perforation
Gastrointestinal disorders		Throat irritation*	Disturbance of taste and smell

*recorded for twice daily dosing for nasal polyposis

†recorded at uncommon frequency for twice daily dosing for nasal polyposis

Paediatric population

In the paediatric population, the incidence of recorded adverse events in clinical studies, e.g., epistaxis (6%), headache (3%), nasal irritation (2%) and sneezing (2%) was comparable to placebo.

Azelastine Hydrochloride

The following frequencies of undesirable effects were reported for Azelastine nasal spray: ***Commonly (1-10%)***, a substance-specific bitter taste may be experienced after administration (often due to incorrect method of application, namely tilting the head too far backwards during administration) which, in rare cases, may lead to nausea.

Uncommonly (0.1-1%), a mild, transient irritation of the inflamed nasal mucosa may occur with symptoms such as stinging, itching, sneezing and epistaxis.

In very rare cases (<0.01%), hypersensitivity reactions (such as rash, pruritus, urticaria) were reported.

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 requested to report any suspected adverse reactions via national regulatory portal or systems.

4.9 Overdose

No specific information is available on the treatment of overdose with fixed dose combination of Mometasone Furoate and Azelastine Hydrochloride Nasal Spray. Information regarding overdose of individual components is provided below.

Mometasone furoate

Symptoms

Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of HPA axis function.

Management

Because the systemic bioavailability of mometasone nasal spray is <1%, overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage.

Azelastine Hydrochloride

The results of animal studies show that toxic doses can produce CNS symptoms, e.g. excitation, tremor, convulsions. Should these occur in humans, symptomatic and supportive treatment should be instigated as there is no specific antidote. Gastric lavage is recommended if the overdose is recent.

With the nasal route of administration overdosage reactions are not anticipated.

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

Mometasone Furoate and Azelastine Hydrochloride Nasal Spray combines two active substances, which have different modes of action and provide greater efficacy than individual components in terms of improvement of seasonal allergic rhinitis symptoms.

Mometasone furoate

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. 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.

Azelastine Hydrochloride

Azelastine, a phthalazinone derivative of novel structure, is classified as a potent long acting anti-allergic compound with particularly strong H1 antagonist properties.

Pharmacodynamic effects

Mometasone furoate

In studies utilising nasal antigen challenge, mometasone furoate nasal spray has shown anti- inflammatory activity in both the early- and late-phase allergic responses. This has been demonstrated by decreases (vs placebo) in histamine and eosinophil activity and reductions (vs baseline) in eosinophils, neutrophils, and epithelial cell adhesion proteins.

In 28% of the patients with seasonal allergic rhinitis, mometasone furoate nasal spray demonstrated a clinically significant onset of action within 12 hours after the first dose. The median (50%) onset time of relief was 35.9 hours.

Azelastine Hydrochloride

Data from animal studies show that where high levels of azelastine are achieved both inhibition and release of chemical mediators (e.g. leukotriene, histamine, serotonin) involved in allergic reaction occurs.

Paediatric population

In a placebo-controlled clinical trial in which paediatric patients

(n=49/group) were administered mometasone furoate nasal spray 100 micrograms daily for one year, no reduction in growth velocity was observed.

There are limited data available on the safety and efficacy of mometasone furoate nasal spray in the paediatric population aged 3 to 5 years, and an appropriate dosage range cannot be established. In a study involving 48 children aged 3 to 5 years treated with intranasal mometasone furoate 50, 100 or 200 µg/day for 14 days, there was no significant differences from placebo in the mean change in plasma cortisol level in response to the tetracosactrin stimulation test.

Clinical Study - Mometasone Furoate and Azelastine Hydrochloride Nasal Spray

In an open label, randomized, comparative study of 14 days treatment duration, two dosing regimen of Mometasone Furoate and Azelastine Hydrochloride (140 mcg/50 mcg) Nasal Spray were compared with Mometasone Furoate 50 mcg nasal spray monotherapy and Azelastine Hydrochloride 140 mcg nasal spray monotherapy in the treatment of seasonal allergic rhinitis.

The regimens of Mometasone Furoate and Azelastine Hydrochloride (140 mcg/50 mcg) Nasal Spray were one spray in each nostril twice daily or two sprays in each nostril once daily. A total of 560 patients were enrolled in the study. There was a statistically significant difference, reported for the primary end point, mean change in the total nasal symptom score (TNSS) [composite score of rhinorrhoea, nasal congestion, nasal itching and sneezing] between Mometasone Furoate and Azelastine Hydrochloride (140 mcg/50 mcg) Nasal Spray, administered as 1 spray in each nostril twice daily, and each of the monotherapy agents, Azelastine Hydrochloride 140 mcg nasal spray monotherapy, 1 spray per nostril twice daily, and Mometasone Furoate 50 mcg nasal spray monotherapy, 2 sprays per nostril once daily.

5.2 Pharmacokinetic properties

No separate pharmacokinetic study was performed with fixed dose combination of Mometasone Furoate and Azelastine Hydrochloride (140mcg/50mcg) Nasal Spray to characterize its pharmacokinetics.

Absorption

Mometasone Furoate

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.

Azelastine Hydrochloride

After repeated nasal application (0.14 mg) into each nostril twice daily, the plasma levels of azelastine were about 0.26 ng/ml. The levels of the active metabolite desmethylazelastine were detected at or below the lower limit of quantification (0.12 ng/ml).

After repeated oral administration, the mean Cmax steady state plasma levels were determined giving 3.9 ng/ml for azelastine and 1.86 ng/ml for desmethylazelastine after 2.2 mg b.i.d. azelastine which represents the therapeutic oral dose for the treatment of allergic rhinitis.
Following oral administration azelastine is rapidly absorbed showing an absolute bioavailability of 81%. Food has no influence on absorption.

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

Azelastine Hydrochloride
The volume of distribution is high indicating distribution predominantly to the peripheral tissues. The level of protein binding is low (80-95%, a level too low to give concern over drug displacement reactions).

Metabolism
Mometasone Furoate
The small amount of mometasone that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism.

Azelastine Hydrochloride
See below section elimination.

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

Azelastine Hydrochloride
Plasma elimination half-lives after a single dose of azelastine are approximately 20 hours for azelastine and about 45 hours for N-desmethylazelastine (a therapeutically active metabolite). Excretion occurs mainly via the faeces. The sustained excretion of small amounts of the dose in the faeces suggests that some enterohepatic circulation may take place.

5.3 Preclinical safety data

Mometasone furoate + Azelastine HCl Combination

Mometasone Furoate and Azelastine Hydrochloride Nasal Spray (up to

dose of 480/171 mcg/day) when administered intranasally to Wistar rats twice daily for 28 consecutive days did not show any additional toxicity when compared to the toxicity profile of mometasone furoate alone (171 mcg/day) and azelastine hydrochloride alone (480 mcg/day) test in the same study. This represents approximately 10-fold overage to the human total daily dose of 560 µg azelastine hydrochloride and 200 µg mometasone furoate based on nasal surface area (NSA) (rat NSA of 14 cm^2 and human NSA of 160 cm^2).

No studies of carcinogenicity, mutagenicity, or impairment of fertility were conducted with mometasone furoate and azelastine HCl combination; however, studies are available for the individual active components, mometasone furoate and azelastine HCl, as described below.

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, anti- androgenic, estrogenic or anti-estrogenic activity but, like other glucocorticoids, it exhibits some anti-uterotrophic 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 mcg/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 mcg/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.

Azelastine Hydrochloride

Azelastine hydrochloride displayed no sensitising potential in the guinea pig. Azelastine demonstrated no genotoxic potential in a battery of in vitro and in vivo tests, nor any carcinogenic potential in rats or mice.

In male and female rats, azelastine at oral doses greater than 3.0 mg/kg/day caused a dose- related decrease in the fertility index; no substance-related alterations were found in the reproductive organs of males or females during chronic toxicity studies, however.
Embryotoxic and teratogenic effects in rats, mice and rabbits occurred only at maternal toxic doses (for example, skeletal malformations were observed in rats and rabbits at doses of 68.6 mg/kg/day).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Microcrystalline Cellulose & Carboxymethylcellulose Sodium BP, Carmellose Sodium BP, Anhydrous Glucose BP, Citric acid monohydrate BP, Sodium citrate BP, Polysorbate 80 (Super refined Tween 80), Benzalkonium chloride BP, Di-sodium Edetate BP, Neotame USP-NF, Citric acid monohydrate BP, Water for Injection BP

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

24 Months

6.4 Special precautions for storage:

Store below 30°C.

6.5 Nature and contents of container:

A printed carton containing a leaflet and a labeled HDPE plastic bottle filled with white to off white suspension and crimped with nasal spray pump, fitted with an actuator and cap.

6.6 Special precautions for disposal and other handling:

Keep all medicines out of reach of Children. Do not exceed the recommended dose.

7. MARKETING AUTHORISATION HOLDER

Glenmark Pharmaceuticals
Limited, B/2, Mahalaxmi
Chambers,
22 Bhulabhai Desai Road,
Mumbai, 400 026, India

8. MARKETING AUTHORISATION NUMBER(S)

H2015/CTD2901/526

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31-Nov-2015

10. DATE OF LAST REVISION OF THE TEXT

November 2025

11. DATE OF REVISION OF THE TEXT

23RD Jan 2026