SUMMARY OF THE PRODUCT CHARACTERISTICS

MONASAL® Nasal spray 50 µg/spray (Mometasone Furoate)

Eurodrug Laboratories

1. NAME OF THE MEDICINAL PRODUCT

MONASAL® 50 micrograms/actuation nasal spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each delivered dose contains mometasone furoate monohydrate equivalent to 50 micrograms of mometasone furoate anhydrous.

Excipient with known effect:
This medicinal product contains 0.20 mg/g of benzalkonium chloride

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal spray, suspension.
White to off-white viscous suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MONASAL® is indicated for use in adults and children 2 years of age and older to treat the symptoms of seasonal or perennial allergic rhinitis.

In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with MONASAL® is recommended two to four weeks prior to the anticipated start of the pollen season.

MONASAL® is indicated for the treatment of nasal polyps in adults 18 years of age and older. Treatment of nasal polyps in paediatric patients less than 18 years of age has not been established.

MONASAL® is indicated for the treatment of symptoms associated with mild to moderate uncomplicated acute rhinosinusitis in patients 12 years of age and older without signs and symptoms of severe bacterial infection.

4.2 Posology and method of administration

After initial priming of the MONASAL® nasal spray pump, each actuation delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 micrograms mometasone furoate.

Posology
Seasonal or perennial allergic rhinitis
Adults (including older patients) and children 12 years of age and older: The usual recommended dose is two

actuations (50 micrograms/actuation) in each nostril once daily (total dose 200 micrograms). Once symptoms are controlled, dose reduction to one actuation in each nostril (total dose 100 micrograms) may be effective for maintenance. If symptoms are inadequately controlled, the dose may be increased to a maximum daily dose of four actuations in each nostril once daily (total dose 400 micrograms). Dose reduction is recommended following control of symptoms.

Children between the ages of 2 and 11 years: The usual recommended dose is one actuation (50 micrograms/actuation) in each nostril once daily (total dose 100 micrograms).

Mometasone furoate demonstrated a clinically significant onset of action within 12 hours after the first dose in some patients with seasonal allergic rhinitis; however, full benefit of treatment may not be achieved in the first 48 hours. Therefore, the patient should continue regular use to achieve full therapeutic benefit.

Nasal polyposis
The usual recommended starting dose for polyposis is two actuations (50 micrograms/actuation) in each nostril once daily (total daily dose of 200 micrograms). If after 5 to 6 weeks symptoms are inadequately controlled, the dose may be increased to a daily dose of two sprays in each nostril twice daily (total daily dose of 400 micrograms). The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. If no improvement in symptoms is seen after 5 to 6 weeks of twice daily administration, the patient should be re-evaluated and treatment strategy reconsidered.

Efficacy and safety studies mometasone furoate for the treatment of nasal polyposis were four months in duration.

Paediatric population
Seasonal or perennial allergic rhinitis
The safety and efficacy of mometasone furoate in children under 2 years of age have not been established.

Nasal polyposis
The safety and efficacy of mometasone furoate in children and adolescents under 18 years of age have not been established.

Treatment of acute rhinosinusitis:

Use in adults and children 12 years of age and older: The usual recommended dose is two sprays (50 micrograms/spray) into each nostril twice daily (total daily dose of 400 micrograms). If no improvement in symptoms is seen after 15 days of twice daily administration, you should contact your doctor to discuss other treatments to replace MONASAL®. If symptoms get worse during treatment you should contact your doctor.

Method of administration
Prior to administration of the first dose, shake container well and actuate the pump 10 times (until a uniform spray is obtained). If the pump is not used for 14 days or longer, reprime the pump with 2 actuations until a uniform spray is observed, before next use.

Shake container well before each use. 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 substance, mometasone furoate, or to any of the excipients listed in section 6.1.

MONASAL® 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

Immunosuppression
MONASAL® 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 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 MONASAL® 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 MONASAL® or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuing MONASAL®.

MONASAL® is not recommended in case of nasal septum perforation (see section 4.8).

In clinical studies, epistaxis occurred at a higher incidence compared to placebo. Epistaxis was generally self-limiting and mild in severity (see section 4.8).

MONASAL® contains benzalkonium chloride which may cause irritation or swelling inside the nose, especially if used for a long time.

Use in acute rhinosinusitis

If signs and symptoms of severe bacterial infection are observed (such as fever, persistent severe unilateral facial/tooth pain, orbital or periorbital facial swelling, or worsening of symptoms after an initial improvement), the patient should be advised to consult their physician immediately. If these signs and symptoms are present at the time of diagnosis, treatment with MONASAL® should not be initiated.
Safety and efficacy of MONASAL® Nasal Spray for the treatment of symptoms of acute rhinosinusitis in children under 12 years of age have not been studied.

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 (see section 4.8).

However, patients who are transferred from long-term administration of systemically active corticosteroids to MONASAL® 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, systemic corticosteroid administration should be resumed and other modes of therapy and appropriate measures instituted. During transfer from systemic corticosteroids to MONASAL®, some patients may experience symptoms of withdrawal from systemically active corticosteroids (e.g., joint and/or muscular pain, lassitude, and depression initially) despite relief from nasal symptoms and will require encouragement to continue MONASAL® therapy. 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 mometasone furoate 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 MONASAL® 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.

Visual disturbance
Visual disturbance may be reported with systemic and topical 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 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.

4.5 Interactions with other medicaments and other forms of interaction

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.

4.6 Fertility, pregnancy and lactation

Pregnancy
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). As with other nasal corticosteroid preparations, MONASAL® 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.

Breastfeeding
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 MONASAL® therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

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 (see section 5.3).

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

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	Very rare

Infections and infestations		Pharyngitis Upper respiratory tract infection†		
Cardiovascular disorders				Chest pain Palpitation Tachycardia Angiodema
Immune system disorders			Hypersensitivity including anaphylactic reactions, angioedema,	
Nervous system disorders		Headache		
Eye disorders			Glaucoma Increased intraocular pressure Cataracts Vision, blurred (see also section 4.4)	
Respiratory, thoracic and mediastinal disorders	Epistaxis*	Epistaxis Nasal burning Nasal irritation Nasal ulceration	Nasal septum perforation	
Gastrointestinal disorders		Throat irritation*	Disturbances 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.

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.

4.9 Overdose

Symptoms

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

Management

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

5. PHARMACOLOGICAL PROPERTIES

1.1 Pharmacodynamic properties

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.

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.

Pharmacodynamic effects
In studies utilising nasal antigen challenge, mometasone furoate 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.

Three studies were conducted to assess the safety and efficacy of Mometasone Aqueous Nasal Spray in the treatment of nasal polyps for four month. These included two pivotal trials evaluating doses of 200mcg once or twice daily and a supportive trial evaluating a dose of 200mcg once daily. A total of 594 adult patients (ages 18 to 86 years) received Mometasone Aqueous Nasal Spray. The co-primary efficacy endpoints in the pivotal trials were 1) change from baseline in nasal congestion/obstruction averaged over the first month of treatment; and 2) change from baseline to last assessment in bilateral polyp grade during the entire 4 months of treatment as assessed by nasal endoscopy. Efficacy was demonstrated in both studies at a dose of 200mcg twice daily and in one study at a dose of 200mcg once a day. Improvement in other symptoms of nasal polyps (loss of smell, rhinorrhea and postnasal drip) was also observed after a 1-month treatment with 200mcg, twice daily dose compared to placebo in both studies and in one study after once daily treatment. In the supportive study, patients demonstrated a statistically significant improvement with Mometasone Aqueous nasal spray at a dose of 200mcg once a day in relief of nasal congestion and reduction of polyp size with 4 months of treatment compared to placebo.

In two trials with 1954 patients 12 years of age and older with signs and symptoms of acute rhinosinusitis for 7 to 28 days prior to baseline, MOMETASONE Aqueous Nasal Spray 200 µg twice daily was effective in significantly improving symptoms of rhinosinusitis compared to placebo as evaluated by the Major Symptom Score (MSS) composite of symptoms (facial pain/pressure/tenderness, sinus headache, rhinorrhea, post nasal drip, and nasal congestion/stuffiness) during the 15 day treatment period (P02683 $p < 0.001$; P02692 $p = 0.038$). In P02683, MOMETASONE Aqueous Nasal Spray 200µg twice daily reduced the MSS score (averaged across the 15 day treatment period) by 55.6% from baseline, whereas placebo treatment reduced the MSS by 45.6%. In P02692, MOMETASONE Aqueous Nasal Spray 200µg twice daily reduced the MSS score by 48.4% from baseline, whereas placebo treatment reduced the MSS by 41.5% (Table 1).

Table 1 Change from Baseline AM/PM Days 1-15 Major Symptom Score

	Study P02683		Study P02692	
Treatment (n)	MF 200µg BID (233)	Placebo (247)	MF 200µg BID (236)	Placebo (242)
Mean score at baseline	8.29	8.36	7.70	7.72
Mean change in score from baseline	-4.51	-3.75	-3.76	-3.36
Mean% change in score from baseline	-55.6%	-45.6%	-48.4%	-41.5%
P-value vs placebo	<0.001		0.038	

Patients were eligible for study entry only if all signs and symptoms suggestive of bacterial rhinosinusitis were absent. These signs and symptoms were: fever >38.3°C; persistent severe unilateral facial pain or tooth pain; orbital or periorbital facial swelling; dental involvement; and worsening of symptoms after initial improvement. In addition, patients with severe symptoms (on a scale of mild, moderate or severe) in more than three of the five MSS symptom groups were not eligible for study participation. Thus, study subjects generally had mild or moderate rhinosinusitis, likely of non-bacterial origin. Consistent with this, a 500mg three times a day amoxicillin arm was not significantly different from placebo in reducing the symptoms of rhinosinusitis as evaluated by the MSS. Overall, fewer subjects treated with MOMETASONE Aqueous Nasal Spray 200 µg twice daily were considered by the treating physician to be treatment failures than those with placebo (p=0.0074). In addition, during the post-treatment follow-up period, the number of recurrences seen with MOMETASONE was low and comparable to the amoxicillin and placebo treatment groups. Treatment duration beyond 15 days was not evaluated in acute rhinosinusitis.

Paediatric population
In a placebo-controlled clinical trial in which paediatric patients (n=49/group) were administered mometasone furoate 100 micrograms daily for one year, no reduction in growth velocity was observed.

1.2 Pharmacokinetic properties

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.

5.1 Preclinical safety data

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Glycerol
Polysorbate 80
Microcrystalline cellulose and carmellose sodium
Citric acid monohydrate
Sodium citrate
Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.
Use within 2 months of first use.

6.4 Special precautions for storage

Keep this medicine out of the reach and sight of children.

Do not use this medicine after the expiry date which is stated on the bottle and carton after ‘’Exp’’.

The expiry date refers to the last day of that month.

Store the nasal spray below 30°C. Store away from heat. Do not freeze it.

Each bottle should be used within 2 months of first opening. Only open one bottle at a time.

Do not throw away any medicines via wastewater or household waste

6.5 Nature and contents of container

MONASAL® is contained in a white, high density polyethylene bottle, that contains 18 g (140 actuations) of product formulation, supplied with a metering pump and on which a nasal applicator with cap is fitted.

Pack size:
For 18 g : 1 bottle

6.6 Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORISATION HOLDER

Euro Asia Medico Pte. Ltd
6 Tagore drive #04-13 ,Tagore building,
Singapore 787623

8. MANUFACTURER

Manufactured under license for:
Eurodrug Laboratories S.A.,(Belgium)

By FARMEA
10, rue Bouché, Thomas, Z.A.C d'Orgemont,49000
Angers,France

9. DATE OF REVISION OF THE TEXT

March 2020