SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MOMETIX AQ NASAL SPRAY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

Mometasone furoate monohydrate 50 mcg/ actuation

Excipients:

Benzalkonium chloride 0.2 mg/g

Each actuation gives a suspension of 100 mg equivalent of 50 micrograms of mometasone furoate.

3. PHARMACEUTICAL FORM

Non-pressurized multiple uses metered dose aqueous nasal spray suspension. White-off homogenous aqueous suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MOMETIX is used in adults and children aged 6 and older to treat the symptoms of seasonal and perennial rhinitis.

It is used for prophylactic treatment seasonal allergic rhinitis in adults and children aged 12 and older.

MOMETIX can be used in children who have received diagnosis of allergic rhinitis, between 2-6 years old.

Prophylactic treatment may be initiated 2-4 weeks prior to the anticipated start of the pollen season.

In adults aged 18 and over, MOMETIX is also used to treat related symptoms of nasal polyps including congestion and loss of sense of smell.

4.2 Posology and method of administration

For the usage of the first time, or if the spray pump has not been used for 14 days or more, to adjust the spray pump the medication should be sprayed 10 times, usually until uniform spray is observed. Each actuation delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 micrograms

mometasone furoate. If the spray pump has not been used for 14 days or longer, it should be reprimed with 2 actuations, until a uniform spray is observed, before next use.

Seasonal or Perennial Allergic Rhinitis

- Adults (including geriatric patients) and adolescents:

The usual recommended dose is two actuations (50 micrograms / 1 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 Nasal Spray 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

- Adults (including geriatric patients) and children 18 years of age and older:

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, alternative therapies should be considered.

Efficacy and Safety studies of Mometasone furoate Nasal Spray for the treatment of nasal polyposis were four months in duration.

Method of administration

MOMETIX is applied by spraying into nostrils.
Prior to administration of the first dose, shake container well and actuate pump 10 times (until a uniform spray is obtained). If pump is not used for 14 days or longer, reprime the pump with 2 actuations until a uniform spray is observed. Shake container well before each use. The bottle should be discarded after the labelled number of actuations or within 2 months of first use.

Additional Information for Special Populations.

Renal/hepatic failure: There is no data for patients with renal/hepatic failure.

Paediatric Population: The systemic effects of nasal corticosteroids can be seen, especially for prolonged use at high doses. Growth retardation has been reported in children receiving licensed doses of nasal corticosteroids. It is recommended that the height of children receiving long-term 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 pediatric specialist.

Geriatric population: Nasal polyposis treatment for the geriatric population is similar to adults.

4.3 Contraindications

MOMETIX should not be used in case of hypersensitivity to any of the components.

MOMETIX should not be used in the presence of untreated localized infection involving the nasal mucosa.

Due to 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

MOMETIX should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections or ocular herpes simplex.

Following 12 months of treatment with MOMETIX 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. As with any long- term treatment, patients using MOMETIX over several months or longer should be examined periodically for possible changes in the nasal mucosa. If localized fungal infection of the nose or pharynx develops, discontinuance of MOMETIX therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may require cessation of treatment with MOMETIX.

Although MOMETIX 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.

There is no evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression following prolonged treatment with MOMETIX. However, patients who are transferred from long-term administration of systemically active corticosteroids to MOMETIX 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 MOMETIX 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 MOMETIX therapy. Such transfer may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

The safety and efficacy of MOMETIX 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.

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.

Following the use of intranasal corticosteroids, instances of nasal septum perforation or increased intraocular pressure have been reported very rarely.
Safety and efficacy of MOMETIX for the treatment of nasal polyposis in children and adolescents under 18 years of age have not been studied.

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).

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.

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.

Excipients:
MOMETIX has 0.2 mg/g benzalkonium chloride which not causes broncospasm.

4.5 Interaction with other medicinal products and other forms of interaction

A clinical interaction study was conducted with loratadine. In these studies, the plasma concentrations of mometasone furoate are unmeasurable with sensitive assays with a lower detection limit of 50 pg / ml.

4.6 Pregnancy and lactation Pregnancy category: C

Woman potential to be pregnant /Contraseption

No adequate data using in woman potential to be pregnant.

Pregnancy:

There are no adequate or well-controlled studies in pregnant women. As with other nasal corticosteroid preparations, when MOMETIX is decided to be used in pregnant women, possible harm to the mother, fetus and baby should be met with expected benefits. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for hypoadrenalism.

Lactation

As with other nasal corticosteroid preparations, when the use of MOMETIX in breastfeeding women is decided, possible harm to the mother, fetus and baby should be met with expected benefits.

Fertility

There are no sufficient data concerning effect of MOMETIX on fertility of human.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥1/1000, < 1/100); rare (≥ 1/10,000, < 1/1000); very rare (< 1/10,000), not known (cannot estimated from the available data).

- Treatment-related adverse events reported in clinical studies for allergic rhinitis in adults and adolescent patients are given below.

Respiratory, thoracic and mediastinal disorders:

Common: Epistaxis, pharyngitis, nasal burning sensation, nasal irritation, nasal ulceration

Skeletal-muscle disorders and connective tissues-bone disorders:

Unknown: Growth reduction in children receiving long term treatment

It is recommended that the height of children receiving long-term treatment with nasal corticosteroids is regularly monitored.

General disorders and administration site conditions:

Common: Headache

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%). The incidence of all other effects was comparable with that of placebo.

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

- Nasal Polyposis: In patients treated for nasal polyposis, the overall incidence of adverse events was comparable to placebo and similar to that observed for patients with allergic rhinitis. Treatment-related adverse events reported in ≥ 1% of patients in clinical studies for polyposis are shown below:

Respiratory, thoracic and mediastinal disorders:

Very common: Epistaxis (200 mcg twice daily)

Common: Upper tract respiratory infection (200 mcg once daily), nose bleeding (200 mcg once daily).

Uncommon: Upper tract respiratory infection (200 mcg twice daily).

Gastrointestinal disorders:

Common: Throat irritation (200 mcg twice daily).

General disorders and administration site conditions:

Common: Headache (200 mcg once or twice daily).

Rare: Immediate hypersensitivity reactions, including bronchospasm and dyspnoea, may occur after intranasal administration of mometasone furoate monohydrate. Very rarely, anaphylaxis and angioedema have been reported.

Very rare: Disturbances of taste and smell have been reported.

As with other intranasal corticosteroids rare cases of nasal septum perforation or glaucoma or/and cataracts have been reported.

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

4.9 Overdose

Because the systemic bioavailability of MOMETIX is <1% (using sensitive assay with a lower quantitation limit of 0.25 pg/ml) overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage. Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of HPA axis function.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and Other Nasal Preparations for Topical Use-Corticosteroids

ATC Code: R01AD09

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 leukotriene 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.

In studies utilizing nasal antigen challenge, MOMETIX 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 eosinophil, neutrophils, and epithelial cell adhesion proteins.

In 28% of the patients with seasonal allergic rhinitis, MOMETIX 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.

In two trials with 1954 patients, MOMETIX 200 mcg administered twice daily demonstrated significant improvement in symptoms associated with acute rhino sinusitis 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 $p= 0.038$). A 500 mg three times a day amoxicillin arm was not significantly different from placebo in reducing these symptoms of acute rhino sinusitis as evaluated by the MSS. The SNOT-20 HRQL showed a significant level of benefit at the 200 mcg twice daily dose of mometasone furoate vs. placebo ($p=0.047$). Treatment duration beyond 15 days was not evaluated in acute rhino sinusitis.

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

There are limited data available on the safety and efficacy of MOMETIX in the pediatric population aged under 2 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.

5.2 Pharmacokinetic properties

General 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. Mometasone furoate suspension is very poorly absorbed from the gastrointestinal tract.

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:

Metabolites are excreted in urine and bile.

Linearity and Non-linearity:

No available data

5.3 Preclinical safety data

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. Teratology studies have been performed in rats, mice and rabbits by oral, topical (dermal) and / or subcutaneous administration. Effects noted were umbilical hernia in rats (≥ 600 micrograms/kg applied), cleft palate in mice (≥ 180micrograms/kg applied) and gallbladder agenesis, umbilical hernia, and flexed front paws in rabbits (≥ 150micrograms/kg applied). 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 Excipients

Microcristalline cellulose - Sodium carboxymethyl cellulose (Avicel RC 591)

Glycerol

Citric acid monohydrate

Sodium citrate dihydrate

Polysorbate 80

Benzalkonium chloride

Purified water

6.2. Incompatibilities

Not applicable.

6.3 Shelf life

24 months. Use within 2 months of first use.

6.4 Special precautions for storage

Mometasone furoate aqueous nasal spray should not be stored above 30°C. Do not freeze.

6.5 Nature and contents of container

Mometasone furoate aqueous nasal spray is supplied in a HDPE bottle fitted with a non- pressurized metered micro pump with nasal adaptor and a dust cap, suspension 18 g (140 actuations).

6.6 Instructions for use and handling

Unused products or waste materials are disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulation".

7. MARKETING AUTHORIZATION HOLDER

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8. REGISTRATION NUMBER

217/76

9. DATE OF INITIAL OR RENEWED REGISTRATION

Date of first authorisation: 31.12.2008

Renewal of the authorisation:

10. DATE OF REVISION OF THE TEXT

04.04.2014