AUSTRALIAN PRODUCT INFORMATION – NASONEX® AQUEOUS NASAL SPRAY 0.05%, ALCOHOL FREE (mometasone furoate monohydrate)

1 NAME OF THE MEDICINE

Mometasone furoate (as monohydrate)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

NASONEX Aqueous Nasal Spray 0.05% is a metered-dose, manual pump spray unit containing a suspension of mometasone furoate. Each actuation delivers approximately 100 mg of mometasone furoate monohydrate suspension, containing mometasone furoate monohydrate equivalent to mometasone furoate 50 micrograms.

NASONEX Aqueous Nasal Spray 0.05% contains mometasone furoate 0.5 mg/g (as the monohydrate).

For the full list of excipients, see Section 6.1 LIST OF EXCIPIEINTS.

3 PHARMACEUTICAL FORM

Nasal Spray, suspension

NASONEX Aqueous Nasal Spray 0.05% does not contain fluorocarbon propellants.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

NASONEX Aqueous Nasal Spray 0.05% is indicated for the treatment of symptoms associated with seasonal allergic rhinitis and perennial allergic rhinitis and the prophylaxis of seasonal allergic rhinitis in adults, adolescents and children between the ages of 3 and 11 years.

NASONEX Aqueous Nasal Spray 0.05% is also indicated for the treatment of nasal polyps in adult patients 18 years of age and older.

NASONEX Aqueous Nasal Spray 0.05% is indicated for the treatment of symptoms associated with acute rhinosinusitis in patients 12 years of age and older without signs or symptoms of severe bacterial infection.

4.2 DOSE AND METHOD OF ADMINISTRATION

DO NOT EXCEED THE RECOMMENDED DOSAGE.

The effect of NASONEX Aqueous Nasal Spray 0.05% is not immediate. Full therapeutic benefit takes a few days to develop. Dosage should be administered as directed and not be taken by the patients at will for symptomatic relief.

Administration to young children should be aided by an adult.

Allergic Rhinitis
In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with NASONEX Aqueous Nasal Spray 0.05% is recommended two to four weeks prior to the anticipated start of the pollen season.

Adults (including geriatric patients) and children 12 years of age and over
The usual recommended dose for prophylaxis and treatment is two sprays (50 micrograms/spray) in each nostril once daily (total daily dose 200 micrograms). Once symptoms are controlled, reducing the dose to one spray in each nostril (total daily dose 100 micrograms) may be effective for maintenance.

After the first dose of NASONEX Aqueous Nasal Spray 0.05%, clinically significant improvement of symptoms was achieved within 12 hours in 28% of a group of patients (n = 190) with seasonal allergic rhinitis (median = 36 hours). However, the 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.

Children between the ages of 3 and 11 years
The usual recommended dose is one spray (50 micrograms/spray) in each nostril once daily (total daily dose 100 micrograms).

Nasal Polyposis
Adults (including geriatric patients) and adolescents 18 years of age and older
The usual recommended dose for polyposis is two sprays (50 micrograms/spray) in each nostril once daily (total daily dose of 200 micrograms). If 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). Dose reduction is recommended following control of symptoms.

Acute rhinosinusitis
The usual recommended dose for acute rhinosinusitis is two sprays (50 micrograms/spray) in each nostril twice daily (total daily dose of 400 micrograms). If no improvement is seen after 15 days of twice daily administration, alternative therapies should be considered. If symptoms worsen during treatment, the patients should be advised to consult their physician.

Instructions to patients
Shake container well before each use. **Do not** pierce the nasal applicator. After the initial priming of the NASONEX Aqueous Nasal Spray 0.05% pump (10 actuations, until a uniform spray is observed), each actuation delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 micrograms of 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 the next use.

Cleaning your nasal spray: It is important to clean your nasal spray regularly, otherwise it may not work properly. Remove the dust cap and gently pull off the nozzle. Wash the nozzle and dust cap in warm water and then rinse under a running tap. **Do not try to unblock the nasal applicator by inserting a pin or other sharp object as this will damage the applicator and cause you not to get the right dose of medicine.** Allow to dry in a warm place. Push the nozzle back onto the bottle and replace the dust cap. The spray will need to be re-primed with 2 sprays when first used after cleaning.

4.3 CONTRAINDICATIONS

- Patients with known hypersensitivity to mometasone furoate or any of the excipients
- Severe nasal infection, especially candidiasis
- Persons with haemorrhagic diathesis or with a history of recurrent nasal bleeding

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Local nasal effects
NASONEX Aqueous Nasal Spray 0.05% should not be used in the presence of untreated localised infection involving the nasal mucosa.

Following 12 months of treatment with NASONEX Aqueous Nasal Spray 0.05%, there was no evidence of atrophy of the nasal mucosa. Mometasone furoate tended to reverse the nasal mucosa closer to a normal histological phenotype. As with any long-term treatment, patients using NASONEX Aqueous Nasal Spray 0.05% 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 NASONEX Aqueous Nasal Spray 0.05% therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuing NASONEX Aqueous Nasal Spray 0.05%.

Following the use of intranasal aerosolised corticosteroids, instances of nasal septum perforation have been reported very rarely.

Recent surgery or trauma
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.

Immunosuppression
NASONEX Aqueous Nasal Spray 0.05% 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, systemic viral infections or ocular herpes simplex.

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.

Systemic Effects of Corticosteroids
Topical corticosteroids may be absorbed in amounts that can have systemic effects. Use of excessive doses may suppress hypothalamic-pituitary-adrenal (HPA) function. Physicians should be alert for evidence of systemic effects, especially in chronically treated patients.

However, there is no evidence of HPA axis suppression following prolonged treatment with NASONEX Aqueous Nasal Spray 0.05%. Patients who are transferred from long-term administration of systemically active corticosteroids to NASONEX Aqueous Nasal Spray 0.05% 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.

Following the use of intranasal aerosolised corticosteroids, increased intraocular pressure has been reported very rarely.

During transfer from systemic corticosteroids to NASONEX Aqueous Nasal Spray 0.05%, 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 NASONEX Aqueous Nasal Spray 0.05% therapy. Such transfer may also unmask pre-existing allergic conditions such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

Visual disturbance
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.

Use in acute rhinosinusitis
If signs or symptoms of severe bacterial infection are observed (such as fever, persistent severe unilateral facial/tooth pain, orbital or peri-orbital 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 NASONEX should not be initiated.

Use in the elderly
None identified.

Paediatric Use
Controlled clinical trials have shown that intranasal corticosteroids may cause a reduction in growth velocity in children. This effect has been observed in the absence of laboratory evidence of HPA axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in children than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with intranasal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with intranasal corticosteroids has not been adequately studied.

Safety and efficacy of NASONEX Aqueous Nasal Spray 0.05% for the treatment of nasal polyposis in children and adolescents less than 18 years of age have not been studied.

Safety and efficacy of NASONEX Aqueous Nasal Spray 0.05% for the treatment of symptoms of acute rhinosinusitis in children under 12 years of age have not been studied**.**

The growth of children receiving intranasal corticosteroids should be monitored routinely (e.g. via stadiometry). The potential growth effects of prolonged treatment should be weighed against the clinical benefits and the availability of safe and effective non-corticosteroid alternatives. To minimise the systemic effects of intranasal corticosteroids, each patient should be titrated to his/her lowest effective dose.

However, no reduction in growth velocity was observed in a placebo-controlled clinical trial in which paediatric patients were administered NASONEX Aqueous Nasal Spray 0.05% 100 micrograms daily for one year. The effects of treatment for periods of greater than one year have not been studied.

Effects on laboratory tests
None identified.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

In a clinical pharmacokinetic study of mometasone furoate coadministered with loratadine, no clinical interactions between loratadine and mometasone were identified.
Mometasone furoate is metabolised by CYP3A4.

Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, ritonavir, cobicistat-containing products) may lead to increased plasma concentrations of corticosteroids and potentially increase the risk for systemic corticosteroid side-effects. Consider the benefit of coadministration versus the potential risk of systemic corticosteroid effects, in which case patients should be monitored for systemic corticosteroid side-effects.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
As with other corticosteroids, at exposure levels associated with marked signs of systemic corticosteroid toxicity, mometasone furoate had progestogenic effects on the female reproductive tract and mammary glands. However, fertility was unimpaired in a reproductive toxicity study carried out in rats.

Use in Pregnancy (Category B3)
In animal studies, small quantities of mometasone furoate were found to cross the placenta barrier. Like other corticosteroids, at doses associated with signs of systemic toxicity, mometasone furoate reduced fetal growth and was teratogenic in mice, rats and rabbits after subcutaneous or topical application. Higher doses had progestogenic effects in pregnant rats, associated with prolonged gestation, dystocia and reduced pup survival.

There are no adequate or well-controlled studies in pregnant women. Low levels of systemic mometasone have been measured following nasal administration of NASONEX Aqueous Nasal Spray 0.05%.

As with other nasal corticosteroid preparations, NASONEX Aqueous Nasal Spray 0.05% should be used in pregnant women only if the potential benefit justifies the potential risk to the mother or fetus. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for hypoadrenalism.

Use in Lactation
After oral administration, small quantities of mometasone furoate and/or its metabolites were transferred into the milk of lactating rats. There are no data on the extent of passage of mometasone furoate and/or its metabolites into the breast milk of women using mometasone furoate nasal spray 0.05%. As with other nasal corticosteroid preparation, NASONEX Aqueous Nasal Spray 0.05% should be used by lactating mother only if the potential benefit justifies any potential risk to the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person’s ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adult Population
Treatment-related local adverse events reported in clinical studies include headache (8%), epistaxis (i.e. frank bleeding, blood-tinged mucus and blood flecks) (8% vs. placebo 5%), nasal burning (2% vs. placebo 3%), nasal irritation (2% vs. placebo 2%), and nasal ulceration (1%), which are typically observed with the use of a corticosteroid nasal spray. Epistaxis was generally self-limiting and mild in severity, and occurred at a comparable or lower incidence compared to other active control nasal corticoids used in clinical studies (up to 15%). The incidence of all other effects was comparable with that of placebo.

Elderly Population
In the elderly, the more common adverse events were epistaxis (12% vs. placebo 5%), headache (9% vs. placebo 6%) and pharyngitis (4% vs. placebo 2%).

Paediatric Population
In the paediatric population, the most common adverse effects were epistaxis (6% vs. placebo 6%), headache (3% vs. placebo 4%), nasal irritation (2% vs. placebo 1%) and sneezing (2% vs. placebo 4%).

Growth suppression has been reported in association with administration of intranasal corticosteroids (see 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, Paediatric Use).

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.

Acute Rhinosinusitis
In patients treated for acute rhinosinusitis, 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 most frequently in the NASONEX 200 micrograms twice daily group include epistaxis (3.7% vs. placebo 2.6%), diarrhoea (2.1% vs. placebo 0.8%), headache (1.7% vs. placebo 2.4%), nausea (1.7% vs. placebo 0.6%) and abdominal pain (1.7% vs. placebo 1.0%).

Other Adverse Effects
Rarely, immediate hypersensitivity reactions (e.g. bronchospasm, dyspnoea) may occur after intranasal administration of mometasone furoate monohydrate. Very rarely, anaphylaxis and angioedema have been reported.

Disturbances of taste and smell have been reported very rarely.

Vision blurred has been reported.

Cataracts have been reported with administration of intranasal corticosteroids (see 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Because the systemic bioavailability of NASONEX Aqueous Nasal Spray 0.05% is low and has been estimated as <1%, overdose is unlikely to require any therapy other than observation. Treatment can be reinitiated at the usual recommended dose.

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

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

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

In studies utilising nasal antigen challenge, NASONEX Aqueous Nasal Spray 0.05% 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.

Clinical trials

ADULT CLINICAL PROGRAM
Allergic Rhinitis
The clinical program evaluated the efficacy and safety of NASONEX Aqueous Nasal Spray 0.05% in the prophylaxis and treatment of seasonal allergic rhinitis and the treatment of perennial allergic rhinitis. Five Phase I clinical studies evaluated the systemic safety and local tolerability of NASONEX. Other clinical studies included:

- One Phase II dose-ranging study conducted to determine the optimum dose for the Phase III program;

- Seven Phase III studies designed to assess the safety and efficacy of NASONEX in treating seasonal allergic rhinitis for 28 days (including two studies which evaluated the prophylactic efficacy of NASONEX in preventing the symptoms of seasonal allergic rhinitis, and two which evaluated inflammatory response markers following nasal provocation with allergens); and

- Five Phase III studies designed to assess the safety and efficacy of NASONEX in the treatment of perennial allergic rhinitis for 12 weeks. Four studies investigated the long term safety and maintenance of therapeutic effect of NASONEX over 52 weeks; one perennial allergic rhinitis study was conducted in the elderly population; and three open-label perennial allergic rhinitis studies included a "variable-dose group" in which the dose of NASONEX varied from 100 to 400 micrograms daily depending on symptoms.

During the course of the Phase II/III clinical program, 3120 patients (12 years of age and older) were treated with NASONEX Aqueous Nasal Spray 0.05%. The majority (65%) of patients was treated with 200 micrograms once daily. The remainder received NASONEX in a dose ranging from 50 micrograms to 800 micrograms once daily. A total of 712 patients were treated with NASONEX for at least 6 months and 350 patients were treated for 12 months or longer.

The results of the efficacy studies demonstrated that NASONEX Aqueous Nasal Spray 0.05% 200 micrograms/day was consistently superior to placebo in relieving the symptoms of both seasonal allergic rhinitis and perennial allergic rhinitis and was of comparable efficacy to other commonly used topical corticosteroid sprays. In the case of seasonal allergic rhinitis it is also superior to placebo in the prophylaxis of symptoms. In the long-term studies in perennial allergic rhinitis there was no evidence of any diminution of its efficacy over time.

After the first dose of NASONEX, clinically significant improvement of symptoms was achieved within 12 hours in 28% of a group of patients (n = 190) with seasonal allergic rhinitis (median = 36 hours). However, the 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 Polyps

Three studies were conducted to assess the safety and efficacy of NASONEX Aqueous Nasal Spray 0.05% in the treatment of nasal polyps for four months. These included two pivotal trials evaluating doses of 200 micrograms once or twice daily and a supportive trial evaluating a dose of 200 micrograms once daily. A total of 594 adult patients (ages 18 to 86 years) received NASONEX Aqueous Nasal Spray 0.05%. 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 endoscopy. Efficacy was demonstrated in both studies at a dose of 200 micrograms twice daily and in one study at a dose of 200 micrograms once a day. Improvement in other symptoms of nasal polyps (loss of smell, rhinorrhoea and postnasal drip) was also observed after a 1-month treatment with the 200micrograms, 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 NASONEX Aqueous Nasal Spray 0.05% at a dose of 200 micrograms once a day in relief of nasal congestion and reduction of polyp size with 4 months of treatment compared to placebo.

Acute Rhinosinusitis

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, NASONEX Aqueous Nasal Spray 0.05% 200 micrograms 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, rhinorrhoea, post nasal drip and nasal congestion/stuffiness) during the 15 day treatment period (P02683 $p < 0.001$; P02692 $p = 0.038$). In P02683, NASONEX Aqueous Nasal Spray 0.05% 200 micrograms 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, NASONEX Aqueous Nasal Spray 0.05% 200 micrograms 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 200 micrograms BID (233)	Placebo (247)	MF 200 micrograms 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 500 mg 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 NASONEX Aqueous Nasal Spray 0.05% 200 micrograms 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 NASONEX was low and comparable to the amoxicillin and placebo treatment groups. Treatment duration beyond 15 days was not evaluated in acute rhinosinusitis.

PAEDIATRIC CLINICAL PROGRAM
The NASONEX paediatric clinical program consisted of three Phase I pharmacology/pharmacodynamic studies, one Phase II dose-ranging study and three Phase III studies. A total of 1084 paediatric patients received NASONEX. The paediatric program was designed to address all relevant safety issues in paediatric patients aged 3 to 11 years. Additionally, the goal of this program was to establish the lowest effective dose and to confirm efficacy in both seasonal allergic rhinitis and perennial allergic rhinitis.

Two of the Phase I studies conducted in children with allergic rhinitis demonstrated no detectable HPA axis suppression at multiple doses of 50 to 200 micrograms /day for 7 days or 14 days. The third Phase I study, a knemometry study, showed no evidence of a reduction in short-term lower leg growth velocity in NASONEX-treated subjects (100 or 200 micrograms/day).

The Phase II dose-ranging study confirmed the lowest effective dose to be 100 micrograms per day in the treatment of seasonal allergic rhinitis. The three Phase III studies were designed to assess efficacy and safety in perennial allergic rhinitis as well as long-term safety, including an assessment of possible long-term effects on growth.

Compared with placebo, NASONEX 100 micrograms once daily significantly reduced the symptoms of seasonal allergic rhinitis and perennial allergic rhinitis in paediatric patients aged between 3 and 11 years. In addition, NASONEX 100 micrograms once daily was not associated with any reduction in growth velocity when administered for one year.

5.2 PHARMACOKINETIC PROPERTIES

Absorption
Systemic bioavailability of mometasone furoate was investigated in 24 healthy volunteers following intranasal administration of 400 micrograms of the suspension. Mometasone was detectable in plasma (at sporadic time points) in only 4 of the 24 subjects, despite the use of a sensitive assay with a limit of quantitation of 50 pg/mL. Thus, there were no relevant pharmacokinetic data for this dosage form.

Systemic absorption of mometasone furoate suspension administered as aqueous nasal spray, 200 micrograms single dose, was measured using a sensitive assay with a lower quantitation limit of 0.25 pg/mL. Mean C max was 5.77 pg/mL (CV% 32) and mean AUC (0-12hr) 29.6 pg.hr/mL (CV% 37). When compared with dose adjusted PK data for IV mometasone

administration from earlier studies with a quantitation limit of 50 pg/mL and longer sampling duration, the estimated relative systemic (or 'absolute') bioavailability is < 1%. The bioavailability of mometasone following intranasal administration is low.

Systemic effects were not detected in adults, adolescents or children following the administration of mometasone furoate aqueous nasal spray.

Mometasone furoate suspension is very poorly absorbed from the gastrointestinal tract, and the small amount that may be swallowed and absorbed undergoes extensive first-pass metabolism prior to excretion in urine and bile.

5.3 PRECLINICALSAFETY DATA

Genotoxicity
Mometasone furoate is not considered to be genotoxic. There was no evidence of mutagenicity in *in vitro* tests which included tests for reverse mutation in *Salmonella typhimurium* and *Escherichia coli* and forward gene mutation in a mouse lymphoma cell line. Limited evidence of clastogenicity was obtained in Chinese Hamster ovary cells, although this finding was not confirmed in a second assay in Chinese Hamster lung cells *in vitro*, nor *in vivo* assays including a chromosomal aberration assay in mouse spermatogonia, a mouse micronucleus assay or in a rat bone marrow clastogenicity assay. Mometasone furoate did not cause DNA damage in rat liver cells.

Carcinogenicity
No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

benzalkonium chloride (as preservative)
citric acid monohydrate
dispersible cellulose
glycerol
polysorbate 80
purified water
sodium citrate dihydrate

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

3 years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store NASONEX Aqueous Nasal Spray 0.05% below 25^{o}C. Do not freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

NASONEX Aqueous Nasal Spray 0.05% is supplied in a HDPE Pump Actuated Metered Dose Aerosol containing mometasone furoate (as the monohydrate) 50 micrograms/actuation; 1 x 40* metered doses, 1 x 65 metered doses (junior pack), 1 x 140 metered doses, and 2 x 140 metered doses.

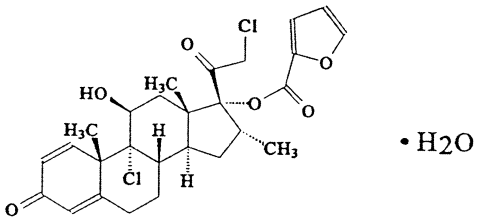
*Not currently marketed in Australia

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



Mometasone furoate monohydrate is 9,21-Dichloro-11ß,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17-(2-furoate) monohydrate. The empirical formula is $C_{27}H_{30}Cl_2O_6 \cdot H_2O$.
MW = 539.45 g/mol.

Mometasone furoate is a white to off white powder and it is practically insoluble in water; slightly soluble in methanol, ethanol and isopropanol; soluble in acetone.

CAS number

CAS Registry number: 83919-23-7 (mometasone furoate anhydrous).

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (Schedule 4)

8 SPONSOR

Merck Sharp & Dohme (Australia) Pty Limited
Level 1 - Building A, 26 Talavera Road
Macquarie Park, NSW 2113, Australia

9 DATE OF FIRST APPROVAL

14 February 2001

10 DATE OF REVISION

21 November 2018

Summary table of changes

Section changed	Summary of new information
4.4	Text relocation and revision of sub-headings
4.5	Addition of information on mometasone and loratadine concomitant administration.
4.5	Addition of potential CYP3A4 drug-drug interaction text.
4.5	Revision of mometasone and loratadine concomitant administration and CYP3A4 TGA proposed text
4.5	Text relocation and revision of sub-headings, revision of CYP3A4 drug-drug interaction text
4.8	Addition of the incidence rate (1%) for a registered adverse effect: 'nasal ulceration'.
4.8	Text relocation and revision of sub-headings
All Sections	PI reformat
All Sections	Minor editorial changes