Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Asmanex Twisthaler 400 micrograms Inhalation Powder

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each delivered dose contains 400 micrograms of mometasone furoate.

Excipients with known effect
The maximum recommended daily dose contains lactose 4.64 mg per day.
For the full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder.
White to off-white powder agglomerates.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Asmanex Twisthaler 400 micrograms Inhalation Powder is indicated in adults and adolescents 12 years of age and older for regular treatment to control persistent asthma.

4.2 Posology and method of administration

Posology
Dosage recommendations are based on severity of asthma (see criteria below).

Patients with persistent mild to moderate asthma: The recommended starting dose for most of these patients is 400 micrograms once daily. Data suggest that better asthma control is achieved if once daily dosing is administered in the evening. Some patients may be more adequately controlled on 400 micrograms daily, given in two divided doses (200 micrograms twice daily). (A formulation of Asmanex Twisthaler 200 micrograms Inhalation Powder is also available.)

The dose of Asmanex Twisthaler 400 micrograms Inhalation Powder should be individualised and titrated to the lowest dose at which effective control of asthma is maintained. Dose reduction to 200 micrograms once daily given in the evening may be an effective maintenance dose for some patients.

Patients with severe asthma: The recommended starting dose is 400 micrograms twice daily, which is the maximum recommended dose. When symptoms are controlled, titrate Asmanex Twisthaler 400 micrograms Inhalation Powder to the lowest effective dose.

In patients with severe asthma and previously receiving oral corticosteroids, Asmanex Twisthaler 400 micrograms Inhalation Powder will be initiated concurrently with the patient's usual maintenance dose of systemic corticosteroid. After approximately one week, gradual withdrawal of the systemic corticosteroid can be initiated by reducing the daily or alternate daily dose. The next reduction is made after an interval of one to two weeks, depending on the response of the patient. Generally, these decrements are not to exceed 2.5 mgof prednisone daily, or its equivalent.

A slow rate of withdrawal is strongly recommended. During withdrawal of oral corticosteroids, patients must be carefully monitored for signs of unstable asthma, including objective measures of airway function, and for adrenal insufficiency (see 4.4). The patient should be instructed that Asmanex Twisthaler 400 micrograms Inhalation Powder is not intended to be used on demand as a reliever medication to treat acute symptoms and that this product mustbe taken regularly to maintain therapeutic benefit even when he or she is asymptomatic.

Criteria:

Mild asthma*: symptoms > 1 time a week but < 1 time per day; exacerbations may affect activity and sleep; night-time asthma symptoms > 2 times a month; PEF or FEV_1 > 80 % predicted, variability 20 – 30 %*
Moderate asthma*: symptoms daily; exacerbations affect activity and sleep; night-time asthma symptoms > 1 time a week; daily use of short-acting $beta_2$–agonist; PEF or FEV_1 > 60-< 80 % predicted, variability > 30 %*
Severe asthma*: continuous symptoms; frequent exacerbations; frequent night-time asthma symptoms; physical activities limited by asthma symptoms; PEF or FEV_1 ≤60% predicted, variability > 30%*

Special populations

Paediatric population
The safety and efficacy of Asmanex Twisthaler 400 mcg in children less than 12 years of age have not been established. No data are available.

Elderly patients older than 65 years of age
No dosage adjustment is necessary.

Method of administration

This product is for inhalation use only.

The patient needs to be instructed how to use the inhaler correctly (see below).
Patients should be in an upright position when inhaling the product.
Prior to removing the cap, be sure the counter and the pointer on the cap are aligned. The inhaler can be opened by removing the white cap while holding unit upright(the maroon-coloured base down), gripping the base, and twisting the cap counterclockwise. The counter will register the number down by one count. Instruct the patient to place the inhaler in the mouth, closing the lips around the mouthpiece, and to breathe in rapidly and deeply. Then, the inhaler is removed from the mouth, and the breath held for about 10 seconds, or as long as is comfortable. The patient is not to breathe out through the inhaler. To close, while holding the unit in an upright position,replace the cap immediately after each inhalation, loading for the next dose by rotating the cap clockwise while gently pressing down until a click sound is heard and the cap is fully closed. The arrow on the cap will be fully aligned with the counter window. After inhalation, patients are advised to rinse the mouth and spit out the water. This helps to reduce the risk of candidiasis.

The digital display will indicate when the last dose has been delivered; after dose 01, the counter will read 00 and the cap will lock, at which time the unit must be discarded. The inhaler is to be kept clean and dry at all times. The outside of the mouthpiece can be cleaned with a dry cloth or tissue; do not wash the inhaler; avoid contact with water.
For detailed instructions see Package Leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section (6.1).

4.4 Special warnings and precautions for use

Oral candidiasis
During clinical trials, oral candidiasis, which is associated with the use of this class of medicinal product, occurred in some patients. This infection may require treatment with appropriate antifungal therapy and in some patients discontinuance of Asmanex Twisthaler 400 micrograms Inhalation Powder may be necessary (see 4.8).

Systemic effects of inhaled corticosteroids
Systemic effects of inhaled 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. Possible systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataracts glaucoma, and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Therefore, it is important that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control of asthma is maintained.

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.

Transferring from systemic corticosteroid therapy
Particular care is needed for patients who are transferred from systemically active corticosteroids to inhaled mometasone furoate, because deaths due to adrenal insufficiency have occurred in asthmatic patients during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) axis function**.**

During dose reduction some patients may experience symptoms of systemic corticosteroid withdrawal, e.g. joint and/or muscular pain, lassitude and depression, despite maintenance or even improvement in pulmonary function. Such patients are to be encouraged to continue with both Asmanex Twisthaler 400 micrograms Inhalation Powder treatment and withdrawal of the systemic corticosteroids, unless objective signs of adrenal insufficiency are present. If evidence of adrenal insufficiency occurs, increase the systemic corticosteroid doses temporarily and thereafter continue withdrawal more slowly.

During periods of stress, including trauma, surgery, or infection, or a severe asthma attack, patients transferred from systemic corticosteroids will require supplementary treatment with a short course of systemic corticosteroids, which is gradually tapered as symptoms subside.
It is recommended that such patients carry a supply of oral corticosteroids and a warning card indicating their need and recommended dosage of systemic corticosteroids during stressful periods. Periodic testing of adrenocortical function, particularly measurement of early morning plasma cortisol levels, is recommended.
Transfer of patients from systemic corticosteroid therapy to Asmanex Twisthaler 400 micrograms Inhalation Powder may unmask pre-existing allergic conditions previously suppressed by systemic corticosteroid therapy. If this occurs, symptomatic treatment is recommended.

Effects on HPA axis function
Use of Asmanex Twisthaler 400 micrograms Inhalation Powder will often permit control of asthma symptoms with less suppression of HPA axis function than therapeutically equivalent oral doses of prednisone. Although mometasone furoate has demonstrated low systemic bioavailability at the recommended dosage, it isabsorbed into the circulation and can be systemically active at higher doses. Thus, to maintain its profile of limited potential for HPA axis suppression, recommended doses of this product must not be exceeded, and must be titrated to the lowest effective dose for each individual patient.

Bronchospasm
As with other inhaled asthma medications, bronchospasm may occur with an immediate increase in wheezing after dosing. If bronchospasm occurs following dosing with the Asmanex Twisthaler 400 micrograms Inhalation Powder, immediate treatment with a fast-acting inhaled bronchodilator is recommended; thus, the patient should be told to keep an appropriate bronchodilator inhaler on hand at all times. In such cases, treatment with Asmanex Twisthaler 400 micrograms Inhalation Powder is then discontinued immediately and alternative therapy instituted.

Mometasone furoate is not to be regarded as a bronchodilator and is not indicated for rapid relief of bronchospasm or asthma attacks; thus, patients should be instructed to keep an appropriate short-actingbronchodilator inhaler on hand for use when needed.

Instruct patients to contact their physician immediately when asthmatic episodes are not responsive to bronchodilators during treatment with this product or if peak-flow falls. This may indicate worsening asthma. During such episodes, patients may require systemic corticosteroid therapy. In these patients, dose titration to the maximum recommended maintenance dose of inhaled mometasone furoate may be considered.

Immunosuppression
Use Asmanex Twisthaler 400 micrograms Inhalation Powder with caution, if at all, in patients with untreated active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections or ocular herpes simplex.

Advise patients who are receiving corticosteroids or other immunosuppressant medicines of the risk of exposure to certain infections (e.g., chickenpox, measles) and of the importance of obtaining medical advice if such exposure occurs. This is of particular importance in children.

Effects on growth

A reduction of growth velocity in children or adolescents may occur as a result of inadequate control of chronic diseases such as asthma or from use of corticosteroids for treatment. Physicians are advised to closely follow the growth of adolescents taking corticosteroids by any route and weigh the benefits of corticosteroid therapy and asthma control against the possibility of growth suppression if an adolescent's growth appears slowed.

If growth is slowed, review therapy with the aim of reducing the dose of inhaled corticosteroids if possible, to the lowest dose at which effective control of symptoms is achieved. In addition, consideration should be given to referring the patient to a paediatric respiratory specialist.

Effects on adrenal suppression
When using inhaled corticosteroids, the possibility for clinically significant adrenal suppression may occur, especially after prolonged treatment with high doses and particularly with higher than recommended doses. This is to be considered during periods of stress or elective surgery, when additional systemic corticosteroids may be needed. However, during clinical trials there was no evidence of HPA axis suppression after prolonged treatment with inhaled mometasone furoate at doses of ≤ 800 micrograms per day.

Dosing considerations
Lack of response or severe exacerbations of asthma should be treated by increasing the maintenance dose of inhaled mometasone furoate, and if necessary, by giving a systemic corticosteroid and/or an antibiotic if infection is suspected, and by use of beta-agonist therapy.
The patient should be advised against abrupt discontinuation of therapy with Asmanex Twisthaler 400 micrograms Inhalation Powder.
There is no evidence that the administration of this product in amounts greater than recommended doses increases efficacy.

Patients with lactose intolerance
The maximum recommended daily dose contains lactose 4.64 mg per day. This amount does not normally cause problems in lactose intolerant people.

4.5 Interaction with other medicinal products and other forms of interactions

Due to the very low plasma concentration achieved after inhaled dosing, clinically significant drug interactions are unlikely. However, there may be a potential for increased systemic exposure to mometasone furoate when strong CYP3A4 inhibitors (eg ketoconazole, itraconazole, nelfinavir, ritonavir, cobicistat) are co-administered. Co-administration of inhaled mometasone furoate with the potent CYP3A4 enzyme inhibitor ketoconazole causessmall but marginally significant (p= 0.09) decreases in serum cortisol AUC $_{(0\text{-}24)}$ and resulted in approximately a 2-fold increase in plasma concentration of mometasone furoate. Interaction studies have only been performed in adults.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects of corticosteroids. 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 with mometasone furoate, like other glucocorticoids, have shown reproductive toxicity (see section 5.3).
As with other inhaled corticosteroid preparations, mometasone furoate is not to be used during pregnancy unless the potential benefit to the mother justifies the potential risk to the mother, fetusor infant. Infants born of mothers who received corticosteroids during pregnancy are to be observed carefully for hypoadrenalism.

Breast-feeding
It is unknown whether mometasone furoate/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in animals have shown excretion of mometasone furoate in milk (see section 5.3). A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from mometasone furoate therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility
In reproductive studies in rats, there was no effect on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Asmanex Twisthaler 400 micrograms Inhalation Powder has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of safety profile

In placebo-controlled clinical trials, oral candidiasis was very common (> 10%) in the 400 micrograms twice daily treatment group; other common (1-10%), treatment-related undesirable effects were pharyngitis, headache and dysphonia. Treatment related undesirable effects seen in the clinical trials and post-marketing reporting with Asmanex Twisthaler Inhalation Powder use are listed below.

Tabulated list of adverse reactions

The adverse reactions reported during clinical trials and the post-marketing period are listed in the following table by treatment regimen, severity, System Organ Class and Preferred Term. Frequencies are defined as 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) and not known (cannot be estimated from the available data).

	QD (Once Daily Dosing)		**BID (Twice Daily Dosing)**	
System Organ Class	**200 mcg**	**400 mcg**	**200 mcg**	**400 mcg**
Infections and infestations				
Candidiasis	common	common	Common	very common
Immune system disorders				
Hypersensitivity reactions including rash, pruritus, angioedema and anaphylactic reaction	not known	not known	not known	not known
Psychiatric disorders				
Psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression	not known	not known	not known	not known
Respiratory, thoracic and mediastinal disorders				
Pharyngitis	common	common	common	common
Dysphonia	uncommon	common	common	common
Asthma aggravation including cough, dyspnea, wheezing and bronchospasm	not known	not known	not known	not known
General disorders and administration site conditions				
Headache	common	common	common	common
Eye disorder	not known	not known	not known	not known
Vision blurred (see also section 4.4)				

In patients dependent on oral corticosteroids, who were treated with Asmanex Twisthaler 400 micrograms twice daily for 12 weeks, oral candidiasis occurred in 20 %, and dysphonia in 7 %. These effects were considered treatment-related.

Uncommonly reported adverse events were dry mouth and throat, dyspepsia, weight increase and palpitations.

As with other inhalation therapy, bronchospasm may occur (see 4.4 Special warnings and precautions for use). This should be treated immediately with a fast-acting inhaled bronchodilator. Asmanex should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

Systemic effects of inhaled corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. These may include adrenal suppression, growth retardation in children and adolescents, and decrease in bone mineral density.

As with other inhaled corticosteroids, rare cases of glaucoma, increased intraocular pressure and/or cataracts have been reported.

As with other glucocorticoid products, the potential for hypersensitivity reactions including rashes, urticaria, pruritus and erythema and oedema of the eyes, face, lips and throat should be considered.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie

4.9 Overdose

Because of the low systemic bioavailability of this product, 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.

Management of the inhalation of mometasone furoate in doses in excess of the recommended dose regimens should include monitoring of adrenal function. Mometasone furoate therapy in a dose sufficient to control asthma can be continued.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:Other Antiasthmatics, Inhalants, - Glucocorticoids, ATC code R03B A07

Mechanism of action
Mometasone furoate is a topical glucocorticoid with local anti-inflammatory properties.
It is likely that much of the mechanism for the effects of mometasone furoate lies in its ability to inhibit the release of mediators of the inflammatory cascade.*In vitro*, mometasone furoate inhibits the release of leukotrienes from leukocytes 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 TNF-alpha; it is also a potent inhibitor of LT production and in addition it is an extremely potent inhibitor of the production of the Th_2 cytokines, IL-4 and IL-5, from human CD4+ T-cells.

Pharmacodynamic effects
Mometasone furoate has been shown *in vitro* to exhibit a binding affinity for the human glucocorticoid receptor which is approximately 12 times that of dexamethasone, 7 times that of triamcinolone acetonide, 5 times that of budesonide, and 1.5 times that of fluticasone.

In a clinical trial, inhaled mometasone furoate has been shown to reduce airway reactivity to adenosine monophosphate in hyperreactive patients. In another trial, pretreatment using the Asmanex Twisthaler for five days significantly attenuated the early and late phase reactions following inhaled allergen challenge and also reduced allergen-induced hyperresponsiveness to methacholine.

Inhaled mometasone furoate treatment was also shown to attenuate the increase in inflammatory cells (total and activated eosinophils) in induced sputum following allergen and methacholine challenge. The clinical significance of these findings is not known.

Clinical efficacy and safety
In asthmatic patients, repeated administration of inhaled mometasone furoate for 4 weeks at doses of 200 micrograms twice daily to 1200 micrograms once daily showed no evidence of clinically relevant HPA-axis suppression at any dose level and was associated with detectable systemic activity only at a dose of 1600 micrograms per day.

In long-term clinical trials using doses up to 800 micrograms per day, there was no evidence of HPA axis suppression, as assessed by reductions in morning plasma cortisol levels or abnormal responses to cosyntropin.

In a 28 day clinical trial involving 60 asthmatic patients, administration of Asmanex Twisthaler at doses of 400 micrograms, 800 micrograms or 1200 micrograms once daily, or 200 micrograms twice daily, did not result in a statistically significant decrease in 24-hour plasma cortisol AUC.

The potential systemic effect of twice daily dosing of mometasone furoate was evaluated in an active and placebo controlled trial that compared 24-hour plasma cortisol AUC in 64 adult asthmatic patients treated for 28 days with mometasone furoate 400 micrograms twice daily, 800 micrograms twice daily, or prednisone 10 mg once daily. Mometasone furoate 400 micrograms twice daily treatment reduced plasma cortisol $AUC_{(0-24)}$ values from placebo values by 10 - 25 %. Mometasone furoate 800 micrograms twice daily reduced plasma cortisol $AUC_{(0-24)}$ from placebo values by 21 - 40 %. Reduction in cortisol was significantly greater after prednisone 10 mg once daily than with placebo or either of the mometasone treatment groups.

Double-blind placebo-controlled trials of 12-weeks duration have shown that treatment with Asmanex Twisthaler at delivered doses within the range of 200 micrograms (once-daily in the evening) - 800 micrograms per day resulted in improved lung function as measured by FEV_1 and peak expiratory flow, improved asthma symptom control, and decreased need for inhaled $beta_{2-}$-agonist. Improved lung function was observed within 24 hours of the start of treatment in some patients, although maximum benefit was not achieved before 1 to 2 weeks or longer. Improved lung function was maintained for the duration of treatment.

5.2 Pharmacokinetic properties

Absorption
The systemic bioavailability of mometasone furoate following oral inhalation in healthy volunteers is low, due to poor absorption from the lungs and the gut and extensive pre-systemic metabolism. Plasma concentrations of mometasone following inhalation at the recommended doses of 200 micrograms to 400 micrograms per day were generally near or below the limit of quantification (50 pg/ml) of the analytical assay and were highly variable.

Distribution
After intravenous bolus administration, the V_d is 332 l. The *in vitro* protein binding for mometasone furoate is high, 98 % to 99 % in concentration range of 5 to 500 ng/ml.

Biotransformation
The portion of an inhaled mometasone furoate dose that is swallowed and absorbed in the gastrointestinal tract undergoes extensive metabolism to multiple metabolites. There are no major metabolites detectable in plasma. In human liver microsomes, mometasone is metabolised by cytochrome P-450 3A4 (CYP3A4).

Elimination
After intravenous bolus administration, mometasone furoate has a terminal elimination $T_{1/2}$ of approximately 4.5 hours. A radiolabelled, orally inhaled dose is excreted mainly in the feces (74 %) and to a lesser extent in the urine (8 %).

5.3 Preclinical safety data

Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows.

General Toxicology
All toxicological effects observed are typical of this class of compounds and are related to exaggerated pharmacological effects of glucocorticoids.

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

Reproductive Function
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.

Lactation
Mometasone furoate is excreted in low doses in the milk of suckling rats.

Carcinogenicity
In long-term carcinogenicity studies in mice and rats, inhaled mometasone furoate demonstrated no statistically significant increase in the incidence of tumours.

Genotoxicity
Mometasone furoate showed no genotoxic activity in a standard battery of *in vitro* and *in vivo* tests.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose anhydrous (which contains trace amounts of milk proteins).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

As packaged for sale: 2 years
After first opening: 3 months.

6.4 Special precautions for storage

Store in original package in order to protect from moisture.
Do not refrigerate or freeze.
Do not store above 30°C.

6.5 Nature and contents of container

Multi-dose powder inhaler.
A counter on the device indicates the number of doses remaining.
The 400 microgram powder inhaler is coloured white with a maroon base, and is a multi-component device composed of polypropylene copolymer, polybutylene terephthalate, polyester, acrylonitrile-butadiene-styrene, bromo-butyl rubber and stainless steel. It contains a silica gel desiccant cartridge in the white polypropylene cap. The inhaler device is enclosed in an aluminium foil laminate pouch.

Pack sizes
Pack of 1 pouched inhaler containing 14 delivered doses
Pack of 1 pouched inhaler containing 30 delivered doses
Pack of 1 pouched inhaler containing 60 delivered doses
Pack of 3 individually packed and pouched inhalers with each inhaler containing 60 delivered doses

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Merck Sharp & Dohme Ireland (Human Health) Limited
Red Oak North

South County Business Park
Leopardstown
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1286/039/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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