

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## **1. NAME OF THE MEDICINAL PRODUCT**

AVAMYS 27.5 micrograms/spray, nasal spray suspension

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each spray actuation delivers 27.5 micrograms of fluticasone furoate.

### Excipient with known effect

One actuation delivers 8.25 micrograms of benzalkonium chloride.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Nasal spray, suspension.

White suspension.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Avamys is indicated in adults, adolescents and children (6 years and over)

Avamys is indicated for the treatment of the symptoms of allergic rhinitis.

### **4.2 Posology and method of administration**

#### Posology

##### *Adults and adolescents (12 years and over)*

The recommended starting dose is two spray actuations (27.5 micrograms of fluticasone furoate per spray actuation) in each nostril once daily (total daily dose, 110 micrograms).

Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril (total daily dose 55 micrograms) may be effective for maintenance.

The dose should be titrated to the lowest dose at which effective control of symptoms is maintained.

##### *Children (6 to 11 years of age)*

The recommended starting dose is one spray actuation (27.5 micrograms of fluticasone furoate per spray actuation) in each nostril once daily (total daily dose, 55 micrograms).

Patients not adequately responding to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) may use two spray actuations in each nostril once daily (total daily dose, 110 micrograms).

Once adequate control of symptoms is achieved, dose reduction to one spray actuation in each nostril once daily (total daily dose, 55 micrograms) is recommended.

For full therapeutic benefit regular, scheduled usage is recommended. Onset of action has been observed as early as 8 hours after initial administration. However, it may take several days of treatment to achieve maximum benefit, and the patient should be informed that their symptoms will improve with continuous regular use (see section 5.1). The duration of treatment should be restricted to the period that corresponds to allergenic exposure.

#### *Children under 6 years of age*

The safety and efficacy of Avamys in children under the age of 6 years has not been established. Currently available data are described in section 5.1 and 5.2 but no recommendation on a posology can be made.

#### *Elderly Patients*

No dose adjustment is required in this population (see section 5.2).

#### *Renal Impairment*

No dose adjustment is required in this population (see section 5.2).

#### *Hepatic Impairment*

No dose adjustment is required in patients with hepatic impairment (see section 5.2).

#### Method of administration

Avamys nasal spray is for administration by the intranasal route only.

The intranasal device should be shaken before use. The device is primed by pressing the mist release button for at least six spray actuations (until a fine mist is seen), whilst holding the device upright. Re-priming (approximately 6 sprays until a fine mist is seen) is only necessary if the cap is left off for 5 days or the intranasal device has not been used for 30 days or more.

The device should be cleaned after each use and the cap replaced.

### **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**

#### Systemic corticosteroid effects

Systemic effects of nasal corticosteroid 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).

Treatment with higher than recommended doses of nasal corticosteroids 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.

Fluticasone furoate 110 micrograms once daily was not associated with hypothalamic-pituitary-adrenal (HPA) axis suppression in adult, adolescent or paediatric subjects. However the dose of intranasal fluticasone furoate should be reduced to the lowest dose at which effective control of the symptoms of rhinitis is maintained. As with all intranasal corticosteroids, the total systemic burden of corticosteroids should be considered whenever other forms of corticosteroid treatment are prescribed concurrently.

If there is any reason to believe that adrenal function is impaired, care must be taken when transferring patients from systemic steroid treatment to fluticasone furoate.

### 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.

### Growth retardation

Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. A reduction in growth velocity has been observed in children treated with fluticasone furoate 110 micrograms daily for one year (see section 4.8 and section 5.1). Therefore, children should be maintained on the lowest possible efficacious dose which delivers adequate symptom control (see section 4.2). It is recommended that the growth 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 (see section 5.1).

### Patients on ritonavir

Concomitant administration with ritonavir is not recommended because of the risk of increased systemic exposure of fluticasone furoate (see section 4.5).

### Excipients

This medicinal product contains benzalkonium chloride. Long-term use may cause oedema of the nasal mucosa.

## **4.5 Interaction with other medicinal products and other forms of interaction**

### Interaction with CYP3A inhibitors

Fluticasone furoate is rapidly cleared by extensive first pass metabolism mediated by the cytochrome P450 3A4.

Based on data with another glucocorticoid (fluticasone propionate), that is metabolised by CYP3A4, coadministration with ritonavir is not recommended because of the risk of increased systemic exposure of fluticasone furoate.

Caution is recommended when co-administering fluticasone furoate with potent CYP3A inhibitors including cobicistat-containing products as an increase in the risk of systemic side effects is expected. Co-administration 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. In a drug interaction study of intranasal fluticasone furoate with the potent CYP3A4 inhibitor ketoconazole there were more subjects with measurable fluticasone furoate concentrations in the ketoconazole group (6 of the 20 subjects) compared to placebo (1 out of 20 subjects). This small increase in exposure did not result in a statistically significant difference in 24 hour serum cortisol levels between the two groups.

The enzyme induction and inhibition data suggest that there is no theoretical basis for anticipating metabolic interactions between fluticasone furoate and the cytochrome P450 mediated metabolism of other compounds at clinically relevant intranasal doses. Therefore, no clinical studies have been conducted to investigate interactions of fluticasone furoate on other drugs.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

There are no adequate data from the use of fluticasone furoate in pregnant women. In animal studies glucocorticoids have been shown to induce malformations including cleft palate and intra-uterine growth retardation. This is not likely to be relevant for humans given recommended nasal doses which results in minimal systemic exposure (see section 5.2). Fluticasone furoate should be used in pregnancy only if the benefits to the mother outweigh the potential risks to the foetus or child.

### Breast-feeding

It is unknown whether nasal administered fluticasone furoate is excreted in human breast milk. Administration of fluticasone furoate to women who are breast-feeding should only be considered if the expected benefit to the mother is greater than any possible risk to the child.

### Fertility

There are no fertility data in humans.

## 4.7 Effects on ability to drive and use machines

Avamys has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

### Summary of the safety profile

The most commonly reported adverse reactions during treatment with fluticasone furoate are epistaxis, nasal ulceration and headache. The most serious undesirable effects are rare reports of hypersensitivity reactions, including anaphylaxis (less than 1 case per 1000 patients).

### Tabulated list of adverse reactions

There were over 2700 patients treated with fluticasone furoate in safety and efficacy studies for seasonal and perennial allergic rhinitis. Paediatric exposure to fluticasone furoate in safety and efficacy studies in seasonal and perennial allergic rhinitis included 243 patients 12 to <18 years, 790 patients 6 to <12 years and 241 patients 2 to <6 years.

Data from large clinical trials were used to determine the frequency of adverse reactions. The following convention has been used for the classification of frequencies: Very common  $\geq 1/10$ ; Common  $\geq 1/100$  to  $< 1/10$ ; Uncommon  $\geq 1/1000$  to  $< 1/100$ ; Rare  $\geq 1/10,000$  to  $< 1/1000$ ; Very rare  $< 1/10,000$ ; Not known (cannot be estimated from the available data).

<b><i>Immune system disorders</i></b>	
Rare	Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria.
<b><i>Nervous system disorders</i></b>	

Common	Headache.
Not known	Dysgeusia, ageusia, anosmia
<b><i>Eye disorders</i></b>	
Not known	Transient ocular changes (see Clinical experience), vision blurred (see also section 4.4)
<b><i>Respiratory, thoracic and mediastinal disorders</i></b>	
Very common	*Epistaxis
Common	Nasal ulceration, dyspnoea**
Uncommon	Rhinalgia, nasal discomfort (including nasal burning, nasal irritation, and nasal soreness), nasal dryness.
Very rare	Nasal septum perforation
Not known	Bronchospasm, dysphonia, aphonia
<b><i>Musculoskeletal and connective tissue disorders (Children)</i></b>	
Not known	***Growth retardation (see Clinical experience).

#### Description of selected adverse reactions

##### *Epistaxis*

\*Epistaxis was generally mild to moderate in intensity. In adults and adolescents, the incidence of epistaxis was higher in longer-term use (more than 6 weeks) than in short-term use (up to 6 weeks).

##### *Systemic effects*

Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods (see section 4.4). Growth retardation has been reported in children receiving nasal corticosteroids.

\*\*Dyspnoea cases were reported in more than 1% of patients during clinical trials with fluticasone furoate; similar rates were also observed in placebo groups.

#### Paediatric population

The safety in children under 6 years has not been well established. Frequency, type and severity of adverse reactions observed in the paediatric population are similar to those in the adult population.

##### *Epistaxis*

\*In paediatric clinical studies of up to 12 weeks duration the incidence of epistaxis was similar between patients receiving fluticasone furoate and patients receiving placebo.

##### *Growth retardation*

\*\*\*In a one-year clinical study assessing growth in pre-pubescent children receiving 110 micrograms of fluticasone furoate once daily, an average treatment difference of -0.27 cm per year in growth velocity was observed compared to placebo (see Clinical efficacy and safety).

#### 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 the national reporting system listed in [Appendix V](#).

## **4.9 Overdose**

In a bioavailability study, intranasal doses of up to 2640 micrograms per day were administered over three days with no adverse systemic reactions observed (see section 5.2).  
Acute overdose is unlikely to require any therapy other than observation.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Nasal preparations, corticosteroids. ATC code: R01AD12

#### Mechanism of action

Fluticasone furoate is a synthetic trifluorinated corticosteroid that possesses a very high affinity for the glucocorticoid receptor and has a potent anti-inflammatory action.

#### Clinical efficacy and safety

##### *Seasonal Allergic Rhinitis in adults and adolescents*

Compared with placebo, fluticasone furoate nasal spray 110 micrograms once daily significantly improved nasal symptoms (comprising rhinorrhoea, nasal congestion, sneezing and nasal itching) and ocular symptoms (comprising itching/burning, tearing/watering and redness of the eyes) in all 4 studies. Efficacy was maintained over the full 24-hours dosing period with once daily administration.

Onset of therapeutic benefit was observed as early as 8 hours after initial administration, with further improvement observed for several days afterwards.

Fluticasone furoate nasal spray significantly improved the patients' perception of overall response to therapy, and the patients' disease-related quality of life (Rhinoconjunctivitis Quality of Life Questionnaire – RQLQ), in all 4 studies.

##### *Perennial Allergic Rhinitis in adults and adolescents*

Fluticasone furoate nasal spray 110 micrograms once daily significantly improved nasal symptoms as well as patients' perception of overall response to therapy compared to placebo in three studies.

Fluticasone furoate nasal spray 110 micrograms once daily significantly improved ocular symptoms as well as improving patients' disease-related quality of life (RQLQ) compared to placebo in one study. Efficacy was maintained over the full 24-hour dosing period with once daily administration.

In a two-year study designed to assess the ocular safety of fluticasone furoate (110 micrograms once daily intranasal spray), adults and adolescents with perennial allergic rhinitis received either fluticasone furoate (n=367) or placebo (n=181). The primary outcomes [time to increase in posterior subcapsular opacity ( $\geq 0.3$  from baseline in Lens Opacities Classification System, Version III (LOCS III grade)) and time to increase in intraocular pressure (IOP;  $\geq 7$  mmHg from baseline)] were not statistically significant between the two groups. Increases in posterior subcapsular opacity ( $\geq 0.3$  from baseline) were more frequent in subjects treated with fluticasone furoate 110 micrograms [14 (4%)] versus placebo [4 (2%)] and were transient in nature for ten subjects in the fluticasone furoate group and two subjects in the placebo group. Increases in IOP ( $\geq 7$  mmHg from baseline) were more frequent in subjects treated with fluticasone furoate 110 micrograms: 7 (2%) for fluticasone furoate 110 micrograms once daily and 1 (<1%) for placebo. These events were transient in nature for six subjects in the fluticasone furoate group and one placebo subject. At weeks 52 and 104, 95% of subjects in both treatment groups had posterior subcapsular opacity values within  $\pm 0.1$  of baseline values for each eye and, at week 104,  $\leq 1\%$  of subjects in both treatment groups had  $\geq 0.3$  increase from baseline in posterior subcapsular opacity. At weeks 52 and 104, the majority of subjects (>95%) had IOP values of within  $\pm 5$  mmHg of the baseline value. Increases in posterior subcapsular opacity or IOP were not accompanied by any adverse events of cataracts or glaucoma.

## Paediatric population

### *Seasonal and perennial allergic rhinitis in children*

The paediatric posology is based on assessment of the efficacy data across the allergic rhinitis population in children.

In seasonal allergic rhinitis, fluticasone furoate nasal spray 110 micrograms once daily was effective but no significant differences were observed between fluticasone furoate nasal spray 55 micrograms once daily and placebo on any endpoint.

In perennial allergic rhinitis, fluticasone furoate nasal spray 55 micrograms once daily exhibited a more consistent efficacy profile than fluticasone furoate nasal spray 110 micrograms once daily over 4 weeks' treatment. Post-hoc analysis over 6 and 12 weeks in the same study, as well as 6-week HPA axis safety study, supported the efficacy of fluticasone furoate nasal spray 110 micrograms once daily.

A 6-week study that assessed the effect of fluticasone furoate nasal spray 110 micrograms once daily on adrenal function in children aged 2 to 11 years showed that there was no significant effect on 24-hour serum cortisol profiles, compared with placebo.

A randomised, double-blind, parallel-group, multicenter, one-year placebo-controlled clinical growth study evaluated the effect of fluticasone furoate nasal spray 110 micrograms daily on growth velocity in 474 prepubescent children (5 to 7.5 years of age for girls and 5 to 8.5 years of age for boys) with stadiometry. Mean growth velocity over the 52-week treatment period was lower in the patients receiving fluticasone furoate (5.19 cm/year) compared to placebo (5.46 cm/year). The mean treatment difference was -0.27 cm per year [95% CI -0.48 to -0.06].

### *Seasonal and perennial allergic rhinitis in children (under 6 years)*

Safety and efficacy studies were performed in a total of 271 patients from 2 to 5 years of age in both seasonal and perennial allergic rhinitis, of whom 176 were exposed to fluticasone furoate.

Safety and efficacy in this group has not been well established.

## **5.2 Pharmacokinetic properties**

### Absorption

Fluticasone furoate undergoes incomplete absorption and extensive first-pass metabolism in the liver and gut resulting in negligible systemic exposure. The intranasal dosing of 110 micrograms once daily does not typically result in measurable plasma concentrations (<10 pg/mL). The absolute bioavailability for intranasal fluticasone furoate is 0.50 %, such that less than 1 microgram of fluticasone furoate would be systemically available after administration of 110 micrograms (see section 4.9).

### Distribution

The plasma protein binding of fluticasone furoate is greater than 99 %. Fluticasone furoate is widely distributed with volume of distribution at steady-state of, on average, 608 L.

### Biotransformation

Fluticasone furoate is rapidly cleared (total plasma clearance of 58.7 L/h) from systemic circulation principally by hepatic metabolism to an inactive 17 $\beta$ -carboxylic metabolite (GW694301X), by the cytochrome P450 enzyme CYP3A4. The principal route of metabolism was hydrolysis of the S-fluoromethyl carbothioate function to form the 17 $\beta$ -carboxylic acid metabolite. In vivo studies have revealed no evidence of cleavage of the furoate moiety to form fluticasone.

### Elimination



Elimination was primarily via the faecal route following oral and intravenous administration indicative of excretion of fluticasone furoate and its metabolites via the bile. Following intravenous administration, the elimination phase half-life averaged 15.1 hours. Urinary excretion accounted for approximately 1 % and 2 % of the orally and intravenously administered dose, respectively.

#### Paediatric population

In the majority of patients fluticasone furoate is not quantifiable ( $< 10$  pg/mL) following intranasal dosing of 110 micrograms once daily. Quantifiable levels were observed in 15.1 % of paediatric patients following intranasal dosing of 110 micrograms once daily and only 6.8 % of paediatric patients following 55 micrograms once daily. There was no evidence for higher quantifiable levels of fluticasone furoate in younger children (less than 6 years of age). Median fluticasone furoate concentrations in those subjects with quantifiable levels at 55 micrograms were 18.4 pg/mL and 18.9 pg/mL for 2-5 yrs and 6-11 yrs, respectively.

At 110 micrograms, median concentrations in those subjects with quantifiable levels were 14.3 pg/mL and 14.4 pg/mL for 2-5 yrs and 6-11 yrs, respectively. The values are similar to those seen in adults (12+) where median concentrations in those subjects with quantifiable levels were 15.4 pg/mL and 21.8 pg/mL at 55 micrograms and 110 micrograms, respectively.

#### Elderly

Only a small number of elderly patients ( $\geq 65$  years,  $n=23/872$ ; 2.6 %) provided pharmacokinetic data. There was no evidence for a higher incidence of patients with quantifiable fluticasone furoate concentrations in the elderly, when compared with the younger patients.

#### Renal impairment

Fluticasone furoate is not detectable in urine from healthy volunteers after intranasal dosing. Less than 1 % of dose-related material is excreted in urine and therefore renal impairment would not be expected to affect the pharmacokinetics of fluticasone furoate.

#### Hepatic impairment

There are no data with intranasal fluticasone furoate in patients with hepatic impairment. Data are available following inhaled administration of fluticasone furoate (as fluticasone furoate or fluticasone furoate/vilanterol) to subjects with hepatic impairment that are also applicable for intranasal dosing. A study of a single 400 microgram dose of orally inhaled fluticasone furoate in patients with moderate hepatic impairment (Child-Pugh B) resulted in increased  $C_{max}$  (42 %) and  $AUC(0-\infty)$  (172 %) and a modest (on average 23 %) decrease in cortisol levels in patients compared to healthy subjects. Following repeat dosing of orally inhaled fluticasone furoate/vilanterol for 7 days, there was an increase in fluticasone furoate systemic exposure (on average two-fold as measured by  $AUC_{(0-24)}$ ) in subjects with moderate or severe hepatic impairment (Child-Pugh B or C) compared with healthy subjects. The increase in fluticasone furoate systemic exposure in subjects with moderate hepatic impairment (fluticasone furoate/vilanterol 200/25 micrograms) was associated with an average 34% reduction in serum cortisol compared with healthy subjects. There was no effect on serum cortisol in subjects with severe hepatic impairment (fluticasone furoate/vilanterol 100/12.5 micrograms). Based on these findings the average predicted exposure of 110 micrograms of intranasal fluticasone furoate in this patient population would not be expected to result in suppression of cortisol.

### **5.3 Preclinical safety data**

Findings in general toxicology studies were similar to those observed with other glucocorticoids and are associated with exaggerated pharmacological activity. These findings are not likely to be relevant for humans given recommended nasal doses which results in minimal systemic exposure. No genotoxic effects of fluticasone furoate have been observed in conventional genotoxicity tests. Further, there were no treatment-related increases in the incidence of tumours in two year inhalation studies in rats and mice.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Glucose anhydrous  
Dispersible cellulose  
Polysorbate 80  
Benzalkonium chloride  
Disodium edetate  
Purified water

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 years  
In-use shelf life: 2 months

### **6.4 Special precautions for storage**

Do not refrigerate or freeze.  
Store upright.  
Always keep the cap on.

### **6.5 Nature and contents of container**

14.2 mL Type I or Type III amber bottle (glass) fitted with a metering spray pump.

The medicinal product is available in three pack sizes: 1 bottle of 30, 60 or 120 sprays.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal and other handling**

No special requirements for disposal.

## **7. MARKETING AUTHORISATION HOLDER**

GlaxoSmithKline (Ireland) Limited  
12 Riverwalk, Citywest Business Campus  
Dublin 24, Ireland

**8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/07/434/001

EU/1/07/434/002

EU/1/07/434/003

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 11 January 2008

Date of latest renewal: 17 December 2012

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency: <http://www.ema.europa.eu>

## **ANNEX II**

**A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING  
AUTHORISATION**

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND  
EFFECTIVE USE OF THE MEDICINAL PRODUCT**

## **A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer responsible for batch release

Glaxo Wellcome S.A.  
Avenida de Extremadura 3  
09400 Aranda de Duero  
Burgos  
Spain

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch

## **B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to medical prescription.

## **C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

## **D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING**

**CARTON**

**1. NAME OF THE MEDICINAL PRODUCT**

Avamys 27.5 micrograms/spray nasal spray suspension  
fluticasone furoate

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each spray delivers 27.5 micrograms of fluticasone furoate

**3. LIST OF EXCIPIENTS**

Also contains: Glucose anhydrous, dispersible cellulose, polysorbate 80, benzalkonium chloride, disodium edetate, purified water.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Nasal spray, suspension  
1 bottle - 30 sprays  
1 bottle - 60 sprays  
1 bottle - 120 sprays

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Shake well before use.  
Read the package leaflet before use.  
Nasal use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP In-use shelf life: 2 months



**9. SPECIAL STORAGE CONDITIONS**

Do not refrigerate or freeze  
Store upright.  
Always keep the cap on.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE****11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

GlaxoSmithKline (Ireland) Limited  
12 Riverwalk, Citywest Business Campus  
Dublin 24, Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/07/434/001  
EU/1/07/434/002  
EU/1/07/434/003

**13. BATCH NUMBER**

LOT

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

avamys

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

**18. UNIQUE IDENTIFIER – HUMAN READABLE DATA**

PC  
SN  
NN

<b>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</b> <b>INTRANASAL SPRAY/DEVICE LABEL</b>
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<b>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</b>
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Avamys 27.5 micrograms/spray nasal spray suspension  
fluticasone furoate  
Nasal use

<b>2. METHOD OF ADMINISTRATION</b>
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Read the package leaflet before use

<b>3. EXPIRY DATE</b>
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EXP

<b>4. BATCH NUMBER</b>
------------------------

LOT

<b>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</b>
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30 sprays  
60 sprays  
120 sprays

<b>6. OTHER</b>
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## **B. PACKAGE LEAFLET**

## Package leaflet: Information for the user

### Avamys 27.5 micrograms per spray nasal spray suspension fluticasone furoate

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist or nurse.
- This medicine has been prescribed for you only. Never pass it on to others. It may harm them, even if their signs of illness seem the same as yours.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4

#### **What is in this leaflet**

1. What Avamys is and what it is used for
  2. What you need to know before you use Avamys
  3. How to use Avamys
  4. Possible side effects
  5. How to store Avamys
  6. Contents of the pack and other information
- Step-by-step guide to using the nasal spray

#### **1. What Avamys is and what it is used for**

Avamys (fluticasone furoate) belongs to a group of medicines called *glucocorticoids*. Avamys works to decrease inflammation caused by allergy (*rhinitis*) and therefore reduce symptoms of allergy.

Avamys nasal spray is used to treat symptoms of allergic rhinitis including stuffy, runny or itchy nose, sneezing and watery, itchy or red eyes, in adults and children aged 6 years and over.

Allergy symptoms can occur at specific times of the year and be caused by allergy to pollen from grass or trees (hayfever), or they can occur all year round and be caused by allergy to animals, house-dust mites or moulds to name some of the most common.

#### **2. What you need to know before you use Avamys**

##### **Do not use Avamys**

- **If you are allergic** to fluticasone furoate or any of the other ingredients of this medicine (listed in section 6).

##### **Warnings and precautions**

##### **Children and adolescents**

Do not use in children under 6 years old.

#### Taking Avamys:

- may when taken for a long time cause children to grow more slowly. The doctor will check your child's height regularly, and make sure he or she is taking the lowest possible effective dose.
- may cause eye conditions such as glaucoma (increase in pressure in the eye) or cataracts (clouding of the lens of the eye). Tell your doctor if you had these conditions in the past, or if you notice blurred vision or other visual disturbances while you are taking Avamys.

#### Other medicines and Avamys

Tell your doctor or pharmacist if you are taking, or have recently taken, or might take any other medicines, including medicines obtained without a prescription.

It is especially important to tell your doctor if you are taking, or have recently taken any of the following medicines:

- steroid tablets or injected steroids
- steroid creams
- medicines for **asthma**
- ritonavir or cobicistat, used to treat **HIV**
- ketoconazole, used to treat **fungal infections**

Your doctor will assess whether you should take Avamys with these medicines. Your doctor may wish to monitor you carefully if you are taking any of these medicines as they may increase the side effects of Avamys.

Avamys should not be used at the same time with other nasal sprays containing steroids.

#### Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

**Do not use Avamys if you are pregnant**, or planning to become pregnant, unless your doctor or pharmacist tells you to.

**Do not use Avamys if you are breast feeding** unless your doctor or pharmacist tells you to.

#### Driving and using machines

Avamys is unlikely to affect your ability to drive and use machines.

#### Avamys contains benzalkonium chloride

This medicine contains 8.25 micrograms of benzalkonium chloride per spray (27.5 micrograms).

Benzalkonium chloride may cause irritation or swelling inside of the nose, especially if used for a long time. Tell your doctor or pharmacist if you feel discomfort when using the spray.

### 3. How to use Avamys

Always use this medicine exactly as your doctor or pharmacist has told you. Don't exceed the recommended dose. Check with your doctor or pharmacist if you're not sure.

#### When to use Avamys

- Use once a day
- Use at the same time each day.

This will treat your symptoms throughout the day and night.

**How long Avamys takes to work**

Some people will not feel the full effects until several days after first using Avamys. However, it is usually effective within 8 to 24 hours of use.

**How much to use****Adults and children 12 years and over**

- **The usual starting dose** is 2 sprays in each nostril once every day.
- Once symptoms are controlled you may be able to decrease your dose to 1 spray in each nostril, once every day.

**Children 6 to 11 years**

- **The usual starting dose** is 1 spray in each nostril once a day.
- If symptoms are very bad your doctor may increase the dose to 2 sprays in each nostril once every day until the symptoms are under control. It may then be possible for the dose to be reduced to 1 spray in each nostril once every day.

**How to use the nasal spray**

Avamys has virtually no taste or smell. It is sprayed into the nose as a fine mist. Be careful not to get any spray into your eyes. If you do, rinse your eyes with water.

There is a step-by-step guide to using the nasal spray after Section 6 of this leaflet. Follow the guide carefully to get full benefit from using Avamys

➤ **See *Step-by-step guide to using the nasal spray*, after Section 6.**

**If you use more Avamys than you should**

Talk to your doctor or pharmacist.

**If you forget to use Avamys**

If you miss a dose, take it when you remember.

If it is nearly the time for your next dose, wait until then. Do not take a double dose to make up for a forgotten dose.

If you have any further questions on the use of this medicine, or if you have any discomfort using the nasal spray ask your doctor or pharmacist or nurse.

**4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**Allergic reactions: get a doctor's help straight away**

Allergic reactions to Avamys are rare and affect less than 1 person in 1,000. In a small number of people, allergic reactions can develop into a more serious, even life-threatening problem if not treated. Symptoms include:

- becoming very wheezy, coughing or having difficulty with breathing
- suddenly feeling weak or light-headed (which may lead to collapse or loss of consciousness)
- swelling around the face
- skin rashes or redness.

In many cases, these symptoms will be signs of less serious side effects. **But you must be aware that they are potentially serious** — so, if you notice any of these symptoms: **Contact a doctor as soon as possible.**

**Very common side effects** (may affect more than 1 in 10 people)

- Nosebleeds (generally minor), particularly if you use Avamys for more than 6 weeks continuously.

**Common side effects** (may affect up to 1 in 10 people)

- Nasal ulceration – which may cause irritation or discomfort in your nose. You may also get streaks of blood when you blow your nose.
- Headache.
- Shortness of breath

**Uncommon side effects** (may affect up to 1 in 100 people)

- Pain, burning, irritation, soreness or dryness in the inside of the nose.

**Very rare side effects** (may affect up to 1 in 10,000 people)

- Small holes (perforations) in the ridge inside the nose that separates the nostrils.

**Not known** (frequency cannot be estimated from the available data)

- Slowing of growth in children.
- Blurred vision or temporary changes to vision with long term use.
- Chest tightness causing difficulty in breathing.
- Voice disorder, voice loss
- Taste disorder, taste loss, smell loss

Nasal corticosteroids can affect the normal production of hormones in your body, particularly if you use high doses for a long time. In children this side effect can cause them to grow more slowly than others.

### **Reporting of side effects**

If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Avamys**

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

It is best to store your Avamys nasal spray upright. Always keep the cap on.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of the month. Avamys nasal spray should be used within 2 months after first opening.

Do not refrigerate or freeze.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.



## **6. Contents of the pack and other information**

### **What Avamys contains**

- The active substance is fluticasone furoate. Each spray delivers 27.5 micrograms of fluticasone furoate.
- The other ingredients are glucose anhydrous, dispersible cellulose, polysorbate 80, benzalkonium chloride, disodium edetate, purified water (see section 2).

### **What Avamys looks like and contents of the pack**

The medicine is a white nasal spray suspension contained in an amber glass bottle, fitted with a pump. The bottle is in an off-white plastic casing with a light blue cap and side-actuated lever. The casing has a window for viewing the bottle contents. Avamys is available in pack sizes 30, 60 and 120 sprays. Not all pack sizes may be marketed.

### **Marketing Authorisation Holder**

Marketing authorisation:  
GlaxoSmithKline (Ireland) Limited  
12 Riverwalk, Citywest Business Campus  
Dublin 24, Ireland

### **Manufacturer:**

Glaxo Wellcome S.A.  
Avenida de Extremadura 3  
09400 Aranda de Duero  
Burgos  
Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

#### **België/Belgique/Belgien**

GlaxoSmithKline Pharmaceuticals s.a./n.v.  
Tél/Tel: + 32 (0)10 85 52 00

#### **Luxembourg/Luxemburg**

GlaxoSmithKline Pharmaceuticals s.a./n.v.  
Belgique/Belgien  
Tél/Tel: + 32 (0)10 85 52 00

#### **България**

GlaxoSmithKline (Ireland) Limited  
Тел.: + 359 80018205

#### **Magyarország**

GlaxoSmithKline (Ireland) Limited  
Tel.: + 36 80088309

#### **Česká republika**

GlaxoSmithKline s.r.o.  
Tel: + 420 222 001 111  
cz.info@gsk.com

#### **Malta**

GlaxoSmithKline (Ireland) Limited  
Tel: + 356 80065004

#### **Danmark**

GlaxoSmithKline Pharma A/S  
Tlf: + 45 36 35 91 00  
dk-info@gsk.com

#### **Nederland**

GlaxoSmithKline BV  
Tel: + 31 (0)33 2081100

**Deutschland**

GlaxoSmithKline GmbH & Co. KG  
Tel.: + 49 (0)89 36044 8701  
produkt.info@gsk.com

**Eesti**

GlaxoSmithKline (Ireland) Limited  
Tel: + 372 8002640

**Ελλάδα**

GlaxoSmithKline Μονοπρόσωπη Α.Ε.Β.Ε.  
Τηλ: + 30 210 68 82 100

**España**

GlaxoSmithKline, S.A.  
Tel: + 34 900 202 700  
es-ci@gsk.com

**France**

Laboratoire GlaxoSmithKline  
Tél.: + 33 (0)1 39 17 84 44  
diam@gsk.com

**Hrvatska**

GlaxoSmithKline (Ireland) Limited  
Tel: + 385 800787089

**Ireland**

GlaxoSmithKline (Ireland) Limited  
Tel: + 353 (0)1 4955000

**Ísland**

Vistor hf.  
Sími: +354 535 7000

**Italia**

GlaxoSmithKline S.p.A.  
Tel: + 39 (0)45 7741 111

**Κύπρος**

GlaxoSmithKline (Ireland) Limited  
Τηλ: + 357 80070017

**Latvija**

GlaxoSmithKline (Ireland) Limited  
Tel: + 371 80205045

**Norge**

GlaxoSmithKline AS  
Tlf: + 47 22 70 20 00

**Österreich**

GlaxoSmithKline Pharma GmbH  
Tel: + 43 (0)1 97075 0  
at.info@gsk.com

**Polska**

GSK Services Sp. z o.o.  
Tel.: + 48 (0)22 576 9000

**Portugal**

GlaxoSmithKline – Produtos Farmacêuticos, Lda.  
Tel: + 351 21 412 95 00  
FI.PT@gsk.com

**România**

GlaxoSmithKline (Ireland) Limited  
Tel: + 40 800672524

**Slovenija**

GlaxoSmithKline (Ireland) Limited  
Tel: + 386 80688869

**Slovenská republika**

GlaxoSmithKline (Ireland) Limited  
Tel: + 421 800500589

**Suomi/Finland**

GlaxoSmithKline Oy  
Puh/Tel: + 358 (0)10 30 30 30  
Finland.tuoteinfo@gsk.com

**Sverige**

GlaxoSmithKline AB  
Tel: + 46 (0)8 638 93 00  
info.produkt@gsk.com

**United Kingdom (Northern Ireland)**

GlaxoSmithKline (Ireland) Limited  
Tel: + 44 (0)800 221441  
customercontactuk@gsk.com

**Lietuva**

GlaxoSmithKline (Ireland) Limited

Tel: + 370 80000334

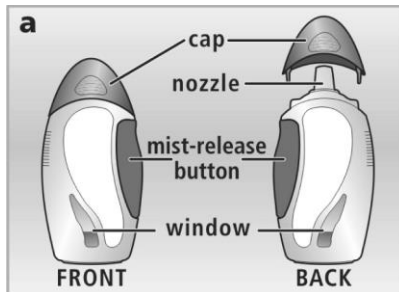
**This leaflet was last revised in**

Detailed information on this medicine is available on the European Medicines Agency website:  
<http://www.ema.europa.eu>

## STEP-BY-STEP GUIDE TO USING THE NASAL SPRAY

### What the nasal spray looks like

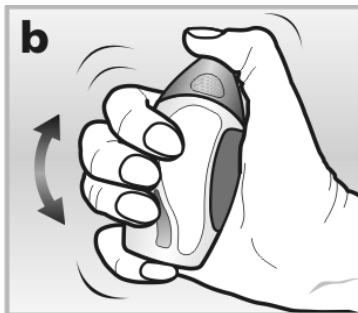
The nasal spray comes in an amber glass bottle inside a plastic casing - see picture **a**. It will contain either 30, 60 or 120 sprays, depending on the pack size that has been prescribed for you.



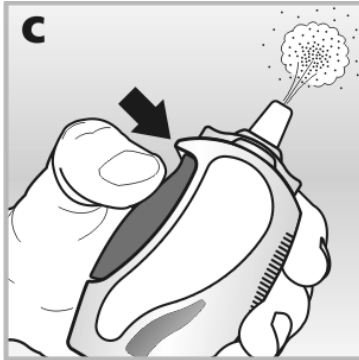
The window in the plastic casing lets you see how much Avamys is left in the bottle. You will be able to see the liquid level for a new 30 or 60 spray bottle, but not in a new 120 spray bottle because the liquid level is above the window.

### Six important things you need to know about using the nasal spray

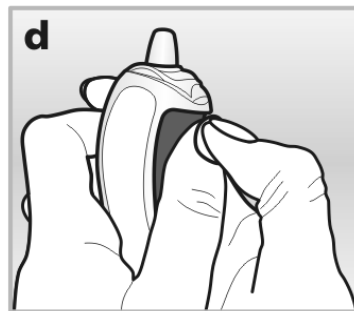
- Avamys comes in an amber glass bottle. If you need to check how much is left **hold the nasal spray upright against a bright light**. You will then be able to see the level through the window.
- When you **first use the nasal spray** you will need to **shake it vigorously** with the cap on for about 10 seconds. This is important as Avamys is a thick suspension that becomes liquid when you shake it well - see picture **b**. It will only spray when it becomes liquid.



- The mist-release button must be **pressed firmly all the way in**, to release the mist through the nozzle - see picture **c**.



- If you have difficulty pressing the button with your thumb, you can use two hands – see picture **d**



- **Always keep the cap on the nasal spray** when you are not using it. The cap keeps the dust out, seals in the pressure and stops the nozzle from blocking up. When the cap is in place the mist-release button cannot be pressed accidentally.
- **Never use a pin** or anything sharp to clear the nozzle. It will damage the nasal spray

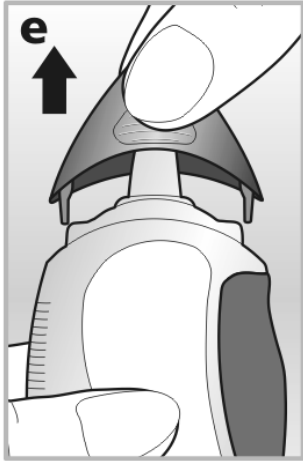
### **Preparing the nasal spray for use**

#### **You must prepare the nasal spray:**

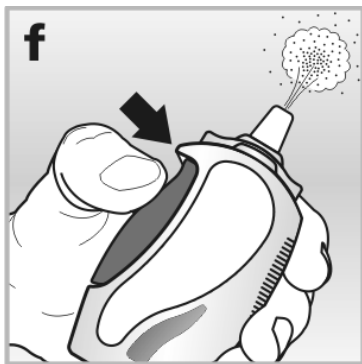
- before you use it for the first time
- if you have left the cap off for 5 days or the intranasal device has not been used for 30 days or more.

Preparing the nasal spray helps to make sure you always get the full dose of medicine. Follow these steps:

- 1 **Shake the nasal spray vigorously** with the cap on for about 10 seconds.
- 2 Remove the cap by squeezing firmly on the sides of the cap with your thumb and forefinger– see picture e.



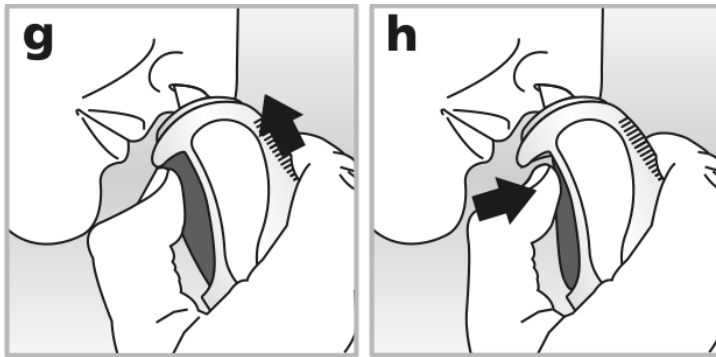
- 3 Hold the nasal spray upright, then tilt and **point the nozzle away from you.**
- 4 **Press the button firmly** all the way in. **Do this at least 6 times** until it releases a fine mist of spray into the air – see picture f.



**The nasal spray is now ready for use.**

### Using the nasal spray

- 1 **Shake the nasal spray vigorously.**
- 2 **Remove the cap.**
- 3 **Blow your nose** to clear your nostrils, then tilt your head forward a little bit.
- 4 Place the nozzle in one of your nostrils – see picture g. Point the end of the nozzle slightly outwards, away from the centre ridge of your nose. This helps to get the medicine to the correct part of your nose.
- 5 Press the **button firmly** all the way in, **while you breathe in through your nose** – see picture h.



- 6 Take the nozzle out and **breathe out through your mouth.**
- 7 If your dose is 2 sprays in each nostril repeat steps 4 to 6.
- 8 Repeat steps 4 to 7 to treat the other nostril.
- 9 **Replace the cap** on the nasal spray.

### Cleaning the nasal spray

#### After each use:

- 1 Wipe the nozzle and inside of the cap with a clean, dry tissue – see pictures **i** and **j**.



- 2 Do not use water to clean it.
- 3 **Never use a pin** or anything sharp on the nozzle.
- 4 **Always replace the cap** once you have finished.

#### If the nasal spray does not seem to be working:

- Check you still have medicine left. Look at the level through the window. If the level is very low there may not be enough left to work the nasal spray.
- Check the nasal spray for damage
- If you think the nozzle may be blocked, **don't use a pin** or anything sharp to clear it.
- Try to reset it by following the instructions under 'Preparing the nasal spray for use'.
- If it is still not working, or if it produces a jet of liquid, take the nasal spray back to the pharmacy to get advice.

**ANNEX IV**

**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE VARIATION TO THE TERMS OF  
THE MARKETING AUTHORISATION(S)**



## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for fluticasone furoate, the scientific conclusions of PRAC are as follows:

In view of available data on dysphonia, aphonia, dysgeusia, ageusia and anosmia from spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between fluticasone furoate and dysphonia, aphonia, dysgeusia, ageusia and anosmia is at least a reasonable possibility. The PRAC concluded that the product information of products containing fluticasone furoate should be amended accordingly.

Having reviewed the PRAC recommendation, the CHMP agrees with the PRAC overall conclusions and grounds for recommendation.

## **Grounds for the variation to the terms of the marketing authorisation(s)**

On the basis of the scientific conclusions for fluticasone furoate the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing fluticasone furoate is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.