For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

AVAMYS NASAL SPRAY

1. GENERIC NAME

Fluticasone Furoate Nasal Spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains:
Fluticasone Furoate 0.05 % w/w
Preservatives: Benzalkonium Chloride Solution IP equivalent to Benzalkonium Chloride 0.015% w/w.
Disodium Edetate IP 0.015% w/w
Each metered dose delivers 27.5 mcg of Fluticasone Furoate

AVAMYS NASAL SPRAY is a white, uniform suspension contained in an amber glass bottle, fitted with a metering (50 microlitres) atomising spray pump. This inner pack is incorporated within a predominantly off-white plastic device with a blue side-actuated lever and a lid which contains a stopper. Each spray of the suspension delivers approximately 27.5 micrograms of micronised fluticasone furoate as an ex-device dose.

3. DOSAGE FORM AND STRENGTH

Nasal spray, suspension.

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4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

For the treatment of symptoms of allergic rhinitis.

4.2.Posology and Method of Administration

AVAMYS NASAL SPRAY is for administration by the intranasal route only. For full therapeutic benefit, regular scheduled usage is recommended. Onset of action has been observed as early as 8 hours after initial administration. It may take several days of treatment to achieve maximum benefit. An absence of an immediate effect should be explained to the patient (*see 5.4 Clinical Studies*).

Populations

For the treatment of seasonal allergic rhinitis and perennial allergic rhinitis:

Adults and Adolescents (12 years and older)

The recommended starting dosage is 2 sprays (27.5 micrograms per spray) in each nostril once daily (total daily dose, 110 micrograms).

Once adequate control of symptoms is achieved, dose reduction to 1 spray in each nostril once daily (total daily dose, 55 micrograms) may be effective for maintenance.

Children (2 to 11 years)

The recommended starting dosage is 1 spray (27.5 micrograms per spray) in each nostril once daily (total daily dose, 55 micrograms).

Patients not adequately responding to 1 spray in each nostril once daily (total daily dose, 55 micrograms) may use 2 sprays in each nostril once daily (total daily dose, 110 micrograms). Once adequate control of symptoms is achieved dose reduction to 1 spray in each nostril once daily (total daily dose, 55 micrograms) is recommended.

Children (under 2 years of age)

There are no data to recommend use of *AVAMYS NASAL SPRAY* for the treatment of seasonal or perennial allergic rhinitis in children under 2 years of age.

Elderly

No dosage adjustment required (*see 5.3 Pharmacokinetic Properties*).

Renal impairment

No dosage adjustment required (*see 5.3 Pharmacokinetic Properties*).

Hepatic impairment

No dosage adjustment is required in patients with hepatic impairment. (see *4.4 Special Warnings and Precautions for Use*, and *5.3 Pharmacokinetic Properties).*

4.3.Contraindications

AVAMYS NASAL SPRAY is contra-indicated in patients with hypersensitivity to any of the ingredients.

4.4.Special Warnings and Precautions for Use

Based on data with another glucocorticoid metabolised by CYP3A4, co-administration with ritonavir is not recommended because of the potential risk of increased systemic exposure to fluticasone furoate (*see 4.5 Drug Interactions* and *5.3 Pharmacokinetic Properties*).

Systemic effects with nasal corticosteroids have been reported, 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. A reduction in growth velocity has been observed in children treated with fluticasone furoate 110 micrograms daily for one year (see 4.8 *Undesirable Effects* and *5.4 Clinical Studies*). Therefore, children should be maintained on the lowest dose which delivers adequate symptom control (see 4.2 *Posology and Method of Administration*). As with other intranasal corticosteroids, physicians should be alert to potential systemic steroid effects including ocular changes such as central serous chorioretinopathy (see 5.4 *Clinical Studies*).

4.5.Drug Interactions

Potential for other drugs to affect pharmacokinetics of fluticasone furoate

Fluticasone furoate is rapidly cleared by extensive first pass metabolism mediated by the cytochrome P450 3A4. In a drug interaction study of intranasal fluticasone furoate with the potent CYP3A4 inhibitor ketoconazole, there were more subjects with measurable fluticasone furoate plasma concentrations in the ketoconazole group (6 of the 20 subjects) compared to placebo (1 of the 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 (*see 4.4 Special Warnings and Precautions for Use, and 5.3 Pharmacokinetic Properties*).

4.6.Use in special Populations (such as pregnant women, lactating women, pediatric patients, geriatric patients, etc.)

Children (2 to 11 years)

The recommended starting dosage is 1 spray (27.5 micrograms per spray) in each nostril once daily (total daily dose, 55 micrograms).

Patients not adequately responding to 1 spray in each nostril once daily (total daily dose, 55 micrograms) may use 2 sprays in each nostril once daily (total daily dose, 110 micrograms). Once adequate control of symptoms is achieved dose reduction to 1 spray in each nostril once daily (total daily dose, 55 micrograms) is recommended.

Children (under 2 years of age)

There are no data to recommend use of *AVAMYS NASAL SPRAY* for the treatment of seasonal or perennial allergic rhinitis in children under 2 years of age.

Elderly

No dosage adjustment required (*see 5.3 Pharmacokinetic Properties*).

Renal impairment

No dosage adjustment required (*see 5.3 Pharmacokinetic Properties*).

Hepatic impairment

No dosage adjustment is required in patients with hepatic impairment. (see 4.4 *Special Warnings and Precautions for Use*, and 5.3 *Pharmacokinetic Properties).*

Pregnancy and Lactation

Adequate data are not available regarding the use of *AVAMYS NASAL SPRAY* during pregnancy and lactation in humans. *AVAMYS NASAL SPRAY* should be used in pregnancy only if the benefits to the mother outweigh the potential risks to the foetus.

Fertility

There are no data in humans (*see 6 Nonclinical Properties, Reproductive Toxicology*).

Pregnancy

Following intranasal administration of *AVAMYS NASAL SPRAY* at the maximum recommended human dose (110 micrograms/day), plasma fluticasone furoate concentrations were typically non-quantifiable and therefore potential for reproductive toxicity is expected to be very low (*see 6 Nonclinical Properties, Reproductive Toxicology*).

Lactation

The excretion of fluticasone furoate into human breast milk has not been investigated.

4.7.Effects on Ability to Drive and Use Machines

Based on the pharmacology of fluticasone furoate and other intranasally administered steroids, there is no reason to expect an effect on ability to drive or to operate machinery with *AVAMYS NASAL SPRAY*.

4.8. Undesirable Effects

Data from large clinical trials were used to determine the frequency of adverse reactions. The following convention has been used for the classification of frequency: 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).

Clinical Trial Data

Respiratory, thoracic and mediastinal disorders

Very common:	Epistaxis
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). In paediatric clinical studies of up to 12 weeks duration the incidence of epistaxis was similar between *AVAMYS NASAL SPRAY* and placebo.	
Common:	Nasal ulceration

Children

Musculoskeletal and connective tissue disorders

Not known:	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 *5.4 Clinical Studies*).	

Post-Marketing Data

Immune system disorders

Rare:	Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria

Nervous system disorders

Common:	Headache.

Respiratory, thoracic and mediastinal disorders

Uncommon:	Rhinalgia, nasal discomfort (including nasal burning, nasal irritation and nasal soreness), nasal dryness.
Very rare:	Nasal septum perforation

4.9.Overdose

Symptoms and Signs

In a bioavailability study, intranasal doses of up to 24 times the recommended daily adult dose were studied over three days with no adverse systemic effects observed (*see 5.3 Pharmacokinetic Properties*).

Treatment

Acute overdose is unlikely to require any therapy other than observation.

5. PHARMACOLOGICAL PROPERTIES

5.1.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.

5.2.Pharmacodynamics Properties

Pharmacodynamic Effects

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

5.3.Pharmacokinetic Properties

Absorption

Fluticasone furoate undergoes extensive first-pass metabolism and incomplete absorption 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 (less than 10 picograms/mL). The absolute bioavailability for fluticasone furoate administered as 880 micrograms three times per day (2640 micrograms total daily dose) is 0.50%.

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.

Metabolism

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.

Special Patient Populations

Elderly

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

Children

Fluticasone furoate is typically not quantifiable (less than 10 picograms /mL) following intranasal dosing of 110 micrograms once daily. Quantifiable levels were observed in less than 16% of paediatric patients following intranasal dosing of 110 micrograms once daily and only less than 7% of paediatric patients following 55 micrograms once daily. There was no evidence for a higher incidence of quantifiable levels of fluticasone furoate in younger children (less than 6 years of age).

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 on intranasal fluticasone furoate in subjects 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-∞) (172%) 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 for 110 micrograms of intranasal fluticasone furoate in this patient population would not be expected to result in suppression of cortisol.

Other pharmacokinetics

Fluticasone furoate is typically not quantifiable (less than 10 picograms/mL) following intranasal dosing of 110 micrograms once daily. Quantifiable levels were only observed in less than 31% of patients aged 12 years and above and in less than 16% of paediatric patients following intranasal dosing of 110 micrograms once daily. There was no evidence for gender, age (including paediatrics), or race to be related to those subjects with quantifiable levels, when compared to those without.

5.4.Clinical Studies

Adult and Adolescent Seasonal Allergic Rhinitis

Once daily 110 micrograms *AVAMYS NASAL SPRAY* resulted in a significant improvement in daily reflective (how patient felt over the preceding 12 hours) and instantaneous (how patient felt at the time of assessment) pre-dose total nasal symptom scores (rTNSS and iTNSS, comprising rhinorrhea, nasal congestion, sneezing and nasal itching) and daily reflective and instantaneous total ocular symptom scores (rTOSS, comprising itching/burning, tearing/watering and redness of the eyes) versus placebo (see table below). The improvement in nasal and ocular symptoms was maintained over the full 24 hours after once daily administration.

Seasonal Allergic Rhinitis: Primary and secondary key endpoints				
Study	**Primary Endpoint: Daily rTNSS**		**Secondary Endpoint: Daily rTOSS**	
	LS Mean Difference	**P-value (95% CI)**	**LS Mean Difference**	**P-value (95% CI)**
FFR20001	-2.012	<0.001 (-2.58, -1.44)	-	-
FFR30003	-0.777	0.003 (-1.28, -0.27)	-0.546	0.008 (-0.95, -0.14)
FFR103184	-1.757	<0.001 (-2.28, -1.23)	-0.741	<0.001 (-1.14, -0.34)
FFR104861	-1.473	<0.001 (-2.01, -0.94)	-0.600	0.004 (-1.01, -0.19)
rTNSS = reflective total nasal symptom scores; rTOSS = reflective total ocular symptom scores; LS = Least square; LS Mean Difference = LS mean change from baseline in active – LS mean change from baseline in placebo; CI = Confidence interval				

The distribution of the patients' perception of overall response to therapy (using a 7-point scale ranging from significantly improved to significantly worse) favoured *AVAMYS NASAL SPRAY* 110 micrograms over placebo, with a statistically significant treatment difference. Onset of action was experienced as early as eight hours after initial administration in two studies. Significant improvement in symptoms was observed in the first 24 hours in all four studies and continued to improve over several days. The patients' quality of life (as assessed by the Rhinoconjunctivitis Quality of Life Questionnaire – RQLQ), was significantly improved from baseline with *AVAMYS NASAL SPRAY* compared to placebo

(Minimum Important Difference in all studies = improvement of at least -0.5 over placebo; treatment difference -0.690, p<0.001, 95% CI -0.84, -0.54).

Adult and Adolescent Perennial Allergic Rhinitis: -

AVAMYS NASAL SPRAY 110 micrograms once daily resulted in a significant improvement in daily rTNSS (LS mean difference = -0.706, P=0.005, 95% CI -1.20, -0.21). The improvement in nasal symptoms was maintained over the full 24 hours after once daily administration. The distribution of patients' perception of overall response to therapy was also significantly improved compared to placebo.

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 (≥0.3 from baseline in Lens Opacities Classification System, Version III (LOCS III grade)) and time to increase in intraocular pressure (IOP; ≥7 mmHg from baseline)] were not statistically significant between the two groups. Increases in posterior subscapsular opacity (≥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 (≥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 ± 0.1 of baseline values for each eye and, at week 104, ≤1% of subjects in both treatment groups had ≥0.3 increase from baseline in posterior subcapsular opacity. At weeks 52 and 104, the majority of subjects (>95%) had IOP values of within ± 5mmHg of the baseline value. Increases in posterior subcapsular opacity or IOP were not accompanied by any adverse events of cataracts or glaucoma.

Children

The paediatric posology is based on assessment of the efficacy data across the allergic rhinitis population in children. In a seasonal allergic rhinitis study in children, *AVAMYS NASAL SPRAY* 110 micrograms over two weeks was effective on primary (daily rTNSS LS mean difference = -0.616, P=0.025, 95% CI -1.15, -0.08) and all secondary nasal endpoints, except the individual reflective score for rhinorrhea. No significant differences were observed between 55 micrograms *AVAMYS NASAL SPRAY* and placebo on any endpoint.

In a perennial allergic rhinitis study, *AVAMYS NASAL SPRAY* 55 micrograms was effective on daily rTNSS (LS mean difference = -0.754, P=0.003, 95% CI -1.24, -0.27). Although there was a trend towards improvement in rTNSS in 100 micrograms, this did not reach statistical significance (LS mean difference = -0.452, P=0.073, 95% CI -1.24, -0.04). Post-hoc analysis of efficacy data over 6 and 12 weeks from this study, and a 6-week HPA-axis safety study, each showed that the improvement in rTNSS for *AVAMYS NASAL SPRAY* 110 micrograms nasal spray over placebo was statistically significant.

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].

6. NONCLINICAL PARTICULARS

6.1.Animal Toxicology or Pharmacology

Findings in general toxicology studies were similar to those observed with other glucocorticoids and are not considered to be clinically relevant to intranasal use of *AVAMYS NASAL SPRAY*.

Carcinogenesis, mutagenesis

There were no treatment-related increases in the incidence of tumours in two-year inhalation studies in rats and mice.

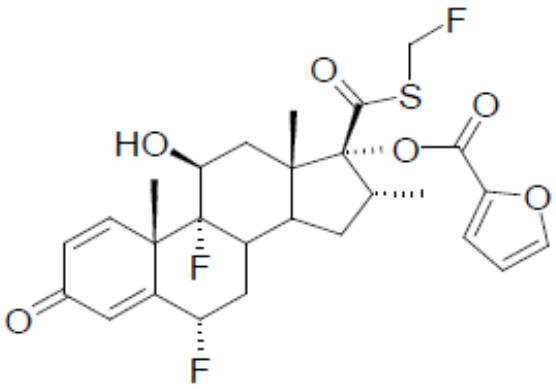
AVAMYS NASAL SPRAY was not genotoxic *in vitro* or *in vivo*.

Reproductive toxicology

The potential for reproductive toxicity was assessed in animals by inhalation administration to ensure high systemic exposure to fluticasone furoate. There were no effects on mating performance or fertility of male or female rats. In rats, developmental toxicity was confined to an increased incidence of incompletely ossified sternabrae in association with lower foetal weight. High doses in rabbits induced abortion. These findings are typical following systemic exposure to potent corticosteroids. There were no major skeletal or visceral abnormalities in either rats or rabbits, and no effect on pre- or post-natal development in rats.

7. DESCRIPTION

Fluticasone furoate, the active component of *AVAMYS NASAL SPRAY*, is a synthetic fluorinated corticosteroid having the chemical name (6α,11β,16α,17α)-6,9-difluoro-17-{[(fluoro-methyl)thio]carbonyl}-11-hydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl 2-furancarboxylate and the following chemical structure:



Fluticasone furoate is a white powder with a molecular weight of 538.6, and the empirical formula is $C_{27}H_{29}F_3O_6S$. It is practically insoluble in water.

AVAMYS NASAL SPRAY is an aqueous suspension of micronized fluticasone furoate for topical administration to the nasal mucosa by means of a metering (50 microliters), atomizing spray pump. After initial priming *(see 4.2 Posology and Method of Administration)*, each actuation delivers 27.5 mcg of fluticasone furoate in a volume of 50 microliters of nasal spray suspension. *AVAMYS NASAL SPRAY* also contains 0.015% w/w benzalkonium chloride, dextrose anhydrous, edetate disodium, microcrystalline cellulose and carboxymethylcellulose sodium, polysorbate 80, and purified water. It has a pH of approximately 6.

8. PHARMACEUTICAL PARTICULARS

List of Excipients

Glucose Anhydrous (also known as Dextrose Anhydrous), Microcrystalline Cellulose and Carboxymethylcellulose Sodium (also known as Dispersible Cellulose), Polysorbate 80, Benzalkonium Chloride Solution, Disodium Edetate (also known as Edetate Disodium), Purified Water.

8.1. Incompatibilities

No incompatibilities have been identified.

8.2. Shelf Life

36 months

The expiry date is indicated on the label and packaging.

8.3. Packaging Information

Nature and Specification of Container

Bottle in a carton.

AVAMYS NASAL SPRAY is a drug suspension contained within a glass bottle fitted with a metering spray pump, which is encased in an off-white plastic device with a blue side-actuated lever and lid.

The fill weight of the products are sufficient to deliver a minimum of 60 or 120 sprays after priming.

All presentations may not be marketed in India.

8.4.Storage and Handling Information

Store below 30ºC.

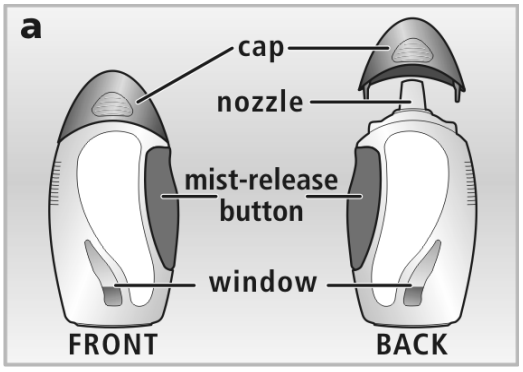
Do not refrigerate or freeze.
Keep out of reach of children

Patients should be instructed that the device must be primed before first use and re-primed if the cap is left off or the device does not seem to be working. In order to prime the device, the nasal spray needs to be shaken vigorously for about 10 seconds with the cap on. This is important as *AVAMYS NASAL SPRAY* is a thick suspension that becomes liquid when vigorously shaken. It will only spray when it becomes liquid. The patient must then press the button firmly all the way in, approximately 6 times until a fine mist is seen (to ensure a full dose is delivered). Once primed, the patient must shake the nasal spray vigorously each time before use. The cap must be replaced after use to keep the nozzle clean and to prevent the need for re-priming. This section includes the following information:

- **The nasal spray**
- **6 important things you need to know about *AVAMYS NASAL SPRAY***
- **Preparing the nasal spray**
- **Using the nasal spray**
- **Cleaning the nasal spray**

The nasal spray

- Your medicine comes in a brown glass bottle inside a plastic casing. It will contain either 60 or 120 sprays, depending on the pack size that has been prescribed for you **(picture a).**



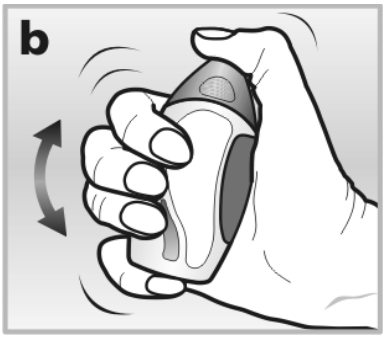
- A window in the plastic casing allows you to see how much medicine is left. You will be able to see the liquid level for a new or 60 spray bottle **(picture a)**, but not for a new 120 spray bottle because the liquid level is above the window.

- The medicine sprays out of the nozzle when the button on the side is **pressed firmly all the way in**.

- A removable cap protects the nozzle from dust and prevents it from blocking up.

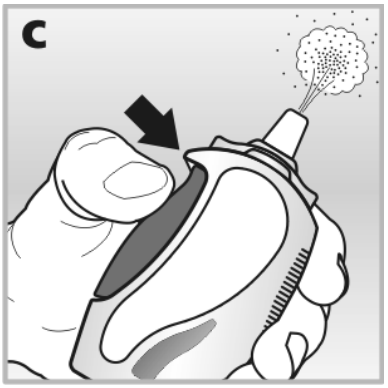
Six important things you need to know about *AVAMYS NASAL SPRAY*

1. The nasal spray comes in a brown glass bottle. 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.



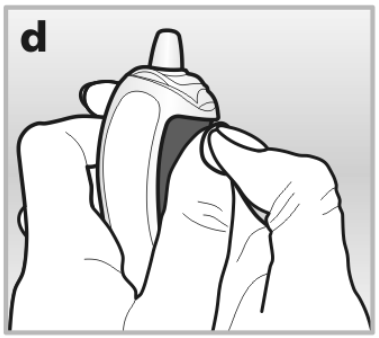
2. When you first use the nasal spray you must shake it vigorously with the cap on for about 10 seconds. This is important as *AVAMYS NASAL SPRAY* is very thick and becomes more liquid when you shake it well (picture b). It will only spray when it becomes liquid.

3. The button on the side must be pressed firmly all the way in, to release a spray through the nozzle (picture c).



4. If you have difficulty pressing the button with your thumb, you can use two hands (picture d).

5. 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 button on the side can't be pressed accidentally.

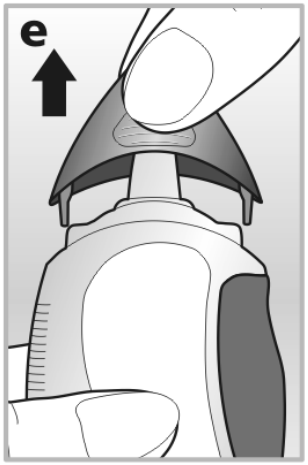


6. Never use a pin or anything sharp to clear the nozzle. It will damage the nasal spray.

Preparing the Nasal Spray

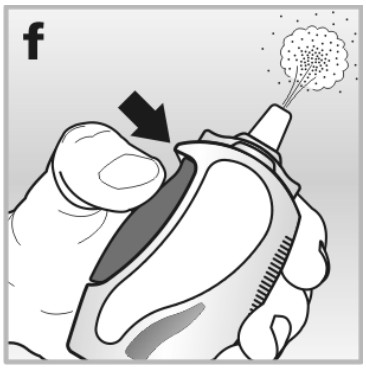
You must prepare the nasal spray:

- **before you use it for the first time**
- **if you have left the cap off.**



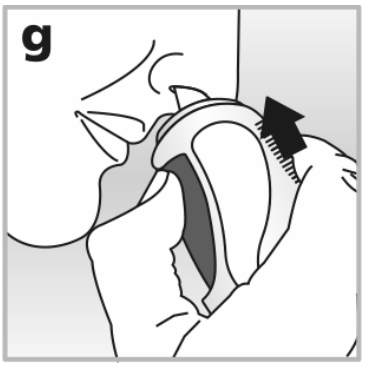
Preparing the nasal spray helps to make sure you always get the full dose of medicine. Follow these steps:

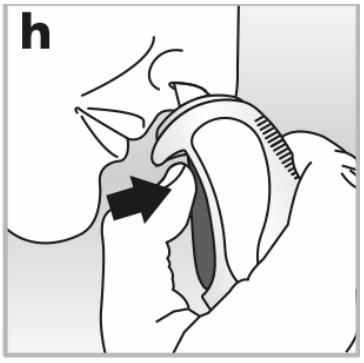
- With the cap on, **shake the nasal spray vigorously** for about 10 seconds.
- Remove the cap by gently squeezing the sides of the cap with your thumb and forefinger and pulling it straight off **(picture e)**.
- Hold the nasal spray upright and point the nozzle away from you.
- **Press the button firmly all the way in. Do this at least 6 times** to release a fine spray into the air **(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, and then tilt your head forward a little bit.
4. Hold the nasal spray upright and carefully place the nozzle in one of your nostrils **(picture g)**.
5. Point the end of the nozzle toward the outside of your nose, away from the centre ridge of your nose. This helps direct the medicine to the right part of your nose.
6. As you breathe in through your nose, **press the button once firmly all the way in (picture h**).
7. Be careful not to get any spray in your eyes. If you do, rinse your eyes with water.



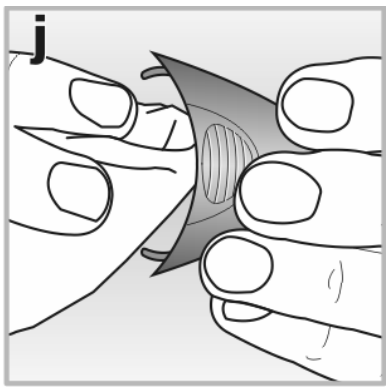


8. Take the nozzle out and breathe out through your mouth.
9. If your doctor has told you to take 2 sprays per nostril, repeat steps 4 to 6.
10. Repeat steps 4 to 6 for your other nostril.
11. **Replace the cap** on the nasal spray.

Cleaning the nasal spray

After each use:

- Wipe the nozzle and the inside of the cap **(picture i and j)**. Don't use water to do this. Wipe with a clean, dry tissue.
- **Never use a pin** or anything sharp on the nozzle.
- **Always replace the cap** once you have finished to keep out dust, seal in the pressure and stop the nozzle from blocking up. 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 anything other than a fine mist (such as a jet of liquid), or if you feel any discomfort using the spray, consult your doctor.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients based on the patient information provided in this section:

This medicine has been prescribed for you personally. Don't pass it on to other people - it may harm them even if their symptoms seem to be the same as yours.
Read the Patient Information that comes with *AVAMYS NASAL SPRAY* carefully before you start using it and each time you get a refill. There may be new information. Keep the leaflet for reference because

it gives you a summary of important information about *AVAMYS NASAL SPRAY*. This leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is *AVAMYS NASAL SPRAY*?

AVAMYS NASAL SPRAY is a medicine that treats seasonal and year-round allergy symptoms in adults and children 2 years old and older.

AVAMYS NASAL SPRAY contains fluticasone furoate, which is a man-made (synthetic) corticosteroid. When you spray *AVAMYS NASAL SPRAY* into your nose, it helps reduce the nasal symptoms of allergic rhinitis (inflammation of the lining of the nose), such as stuffy nose, runny nose, nasal itching, and sneezing. *AVAMYS NASAL SPRAY* may also help red, itchy, and watery eyes in adults and teenagers with seasonal allergic rhinitis.

Your healthcare provider has prescribed *AVAMYS NASAL SPRAY* to treat your symptoms of allergic rhinitis.

It is not known if *AVAMYS NASAL SPRAY* is safe and effective in children under 2 years of age.

Who should not use *AVAMYS NASAL SPRAY*?

Do not use *AVAMYS NASAL SPRAY* if you are allergic to fluticasone furoate or any of the ingredients in *AVAMYS NASAL SPRAY*. See the end of this Patient Information leaflet for a complete list of ingredients in *AVAMYS NASAL SPRAY*.

What should I tell my healthcare provider before taking *AVAMYS NASAL SPRAY*?

Tell your healthcare provider about all of your medical conditions, including if you:

- have had recent nasal sores, nasal surgery, or nasal injury.
- have liver problems.
- have eye or vision problems, such as cataracts or glaucoma (increased pressure in your eye).
- have tuberculosis or any untreated fungal, bacterial, viral infections, or eye infections caused by herpes.
- are exposed to chickenpox or measles.
- are feeling unwell or have any symptoms that you do not understand.
- are pregnant or plan to become pregnant. It is not known if *AVAMYS NASAL SPRAY* will harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if *AVAMYS NASAL SPRAY* can pass into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take *AVAMYS NASAL SPRAY*.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal products. *AVAMYS NASAL SPRAY* and other medicines

may affect each other, causing side effects. Be certain to tell your healthcare provider if you are taking a medicine that contains ritonavir (commonly used to treat HIV infection or AIDS).

How should I use *AVAMYS NASAL SPRAY*?

- This medicine is for use in the nose only. Do not spray it in your eyes or mouth.
- An adult should help a young child use this medicine.
- This medicine has been prescribed for you by your healthcare provider. Do not give this medicine to anyone else.
- Use *AVAMYS NASAL SPRAY* exactly as your healthcare provider tells you to. Do not take more of your medicine or take it more often than your healthcare provider tells you. The prescription label will usually tell you how many sprays to take and how often. If it does not or if you are not sure, ask your healthcare provider.
- For people aged 12 years and older, the usual starting dosage is 2 sprays in each nostril, 1 time a day. After you begin to feel better, your healthcare provider may tell you that 1 spray in each nostril 1 time a day may be enough for you.
- For children aged 2 to 11 years, the usual starting dosage is 1 spray in each nostril, 1 time a day. Your healthcare provider may tell you to take 2 sprays in each nostril 1 time a day. After you begin to feel better, your healthcare provider may change the dosage to 1 spray in each nostril 1 time a day. An adult should help a young child use this medicine.
- Do not use *AVAMYS NASAL SPRAY* after 120 sprays (plus the initial priming sprays) have been used or after the expiration date, whichever comes first. The bottle may not be completely empty. The expiration date is printed as "EXP" on the product label and box. Before you throw away *AVAMYS NASAL SPRAY*, talk to your healthcare provider to see if you need a refill of your prescription. If your healthcare provider tells you to continue using *AVAMYS NASAL SPRAY*,

throw away the empty or expired bottle and use a new bottle of *AVAMYS NASAL SPRAY*. Follow the Instructions for Use below.

- Do not take extra doses or stop taking *AVAMYS NASAL SPRAY* without telling your healthcare provider.
- *AVAMYS NASAL SPRAY* may begin to work within 24 hours after you take your first dose. It may take several days before it has its greatest effect. If your symptoms do not improve or get worse, call your healthcare provider.
- You will get the best results if you keep using *AVAMYS NASAL SPRAY* regularly each day without missing a dose. If you miss a dose by several hours, just take your next dose at the usual time. Do not take an extra dose.

What are the possible side effects of *AVAMYS NASAL SPRAY*?

AVAMYS NASAL SPRAY may cause serious side effects, including:

- thrush (candidiasis), a fungal infection in your mouth and throat. Tell your healthcare provider if you have any redness or white colored patches in your mouth or throat.
- hole in the cartilage in the nose (nasal septal perforation). Symptoms of nasal septal perforation may include:
    - crusting in the nose
    - nosebleeds
    - runny nose
    - whistle sound when you breathe

- slow wound healing. You should not use *AVAMYS NASAL SPRAY* until your nose has healed if you have a sore in your nose, have had surgery on your nose, or if your nose has been injured.
- eye problems such as glaucoma and cataracts. If you have a history of glaucoma or cataracts or have a family history of these eye problems, you should have regular eye exams while you use *AVAMYS NASAL SPRAY*.
- serious allergic reactions. Serious allergic reactions can happen with *AVAMYS NASAL SPRAY*. Stop using *AVAMYS NASAL SPRAY* and call your healthcare provider right away if you have any of the following signs of a serious allergic reaction:
    - shortness of breath or trouble breathing
    - skin rash, redness, or swelling
    - severe itching
    - swelling of the lips, tongue, or face
- immune system problems that may increase your risk of infections. You are more likely to get infections if you take medicines that may weaken your body’s ability to fight infections. Avoid

contact with people who have contagious diseases such as chicken pox or measles while you use *AVAMYS NASAL SPRAY*. Symptoms of an infection may include:
    - fever
    - pain
    - aches
    - chills
    - feeling tired
    - nausea
    - vomiting
- adrenal insufficiency. Adrenal insufficiency is a condition in which the adrenal glands do not make enough steroid hormones. Symptoms of adrenal insufficiency may include:
    - tiredness
    - weakness
    - dizziness
    - nausea
    - vomiting
- slowed or delayed growth in children. A child's growth should be checked regularly while using *AVAMYS NASAL SPRAY*.

The most common side effects of *AVAMYS NASAL SPRAY* include:

- adults and adolescents 12 years of age and older
    - headaches
    - nose bleeds
    - sore throat
    - nose sores
    - back pain

- children 2 to 12 years of age
    - headaches
    - sore throat
    - nose bleeds
    - fever
    - cough

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects of *AVAMYS NASAL SPRAY*. For more information, ask your healthcare provider.

Call your doctor for medical advice about side effects.

What should I know about allergic rhinitis?

"Rhinitis" means inflammation of the lining of the nose. It is sometimes called "hay fever." Allergic rhinitis can be caused by allergies to pollen, animal dander, house dust mite, and mold spores. If you

have allergic rhinitis, your nose becomes stuffy, runny, and itchy. You may also sneeze a lot. You may also have red, itchy, watery eyes; itchy throat; or blocked, itchy ears.

What are the ingredients in *AVAMYS NASAL SPRAY*?

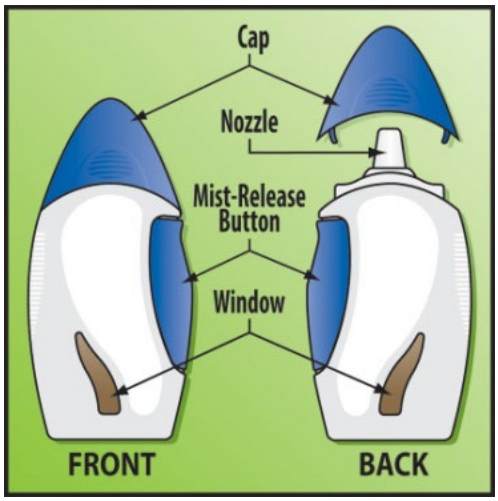
Active ingredient: fluticasone furoate
Inactive ingredients: 0.015% w/w benzalkonium chloride, dextrose anhydrous, edetate disodium, microcrystalline cellulose, carboxymethylcellulose sodium, polysorbate 80, and purified water

Instructions for Use

Read this leaflet carefully before you start to use *AVAMYS NASAL SPRAY*. If you have any questions, ask your healthcare provider.

The parts of the *AVAMYS NASAL SPRAY*

AVAMYS NASAL SPRAY comes in a brown glass bottle inside a nasal device. It contains 120 sprays plus the first priming sprays. Be careful not to drop it. If you accidentally drop the device, check it for damage. If the device is damaged, return it to your pharmacist.



- The Cap has a tab that keeps the Mist-Release Button from being pressed accidentally. It also helps keep the nozzle clean. Do not throw the cap away.
- Always keep the cap on the device when you are not using it.
- The Nozzle is small and short, so it will fit inside your nose. The medicine 5 comes out of the nozzle.
- Pressing the Mist-Release Button sprays a measured amount of medicine from the nozzle as a gentle, fine mist. Because the button is on the side of the device, you can keep the nozzle in the right place in your nose while you press the button.
- The Window lets you see if there is medicine left in the bottle when you hold it in front of a bright light. (You may not be able to see the medicine in a full bottle because the liquid level is above the window.)

How to prime your *AVAMYS NASAL SPRAY*

Priming helps to make sure you always get the same full dose of medicine. You need to prime *AVAMYS NASAL SPRAY*:

- before you use a new bottle for the first time.
- if you have not used your *AVAMYS NASAL SPRAY* for 30 days or longer.
- if the cap has been left off the bottle for 5 days or longer.
- if the device does not seem to be working right.

To prime *AVAMYS NASAL SPRAY*:

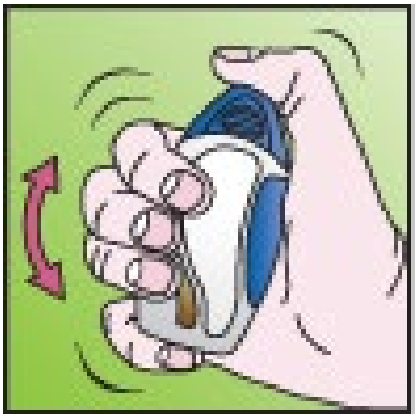


Figure 1

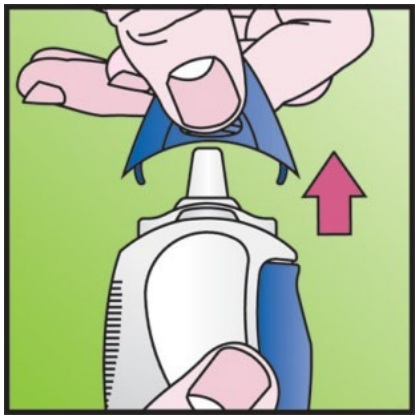


Figure 2

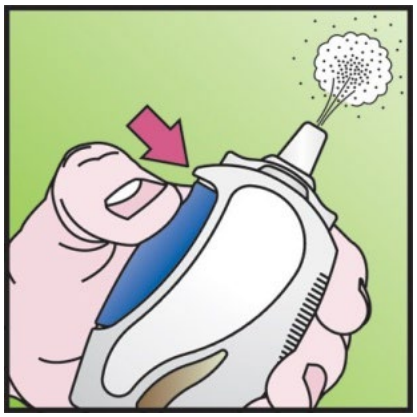


Figure 3

1. With the cap on, shake the device well (Figure 1). This is important to make the medicine a liquid that will spray.
2. Take the cap off by squeezing the finger grips and pulling it straight off (Figure 2).
3. Hold the device with the nozzle pointing up and away from you. Place your thumb or fingers on the button. Press the button all the way in 6 times or until a fine mist sprays from the nozzle (Figure 3). Your *AVAMYS NASAL SPRAY* is now ready to use.

How to use your *AVAMYS NASAL SPRAY*

Follow the instructions below. If you have any questions, ask your healthcare provider .
Before taking a dose of *AVAMYS NASAL SPRAY*, gently blow your nose to clear your nostrils. Shake the bottle well. Then do these 3 simple steps: **Place, Press, Repeat.**

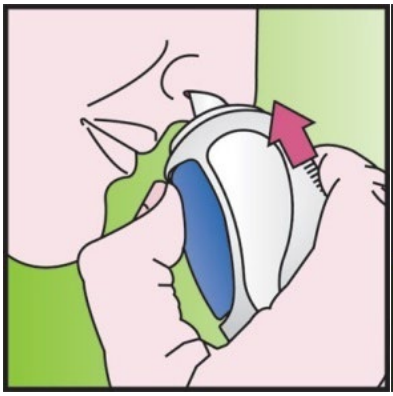


Figure 4

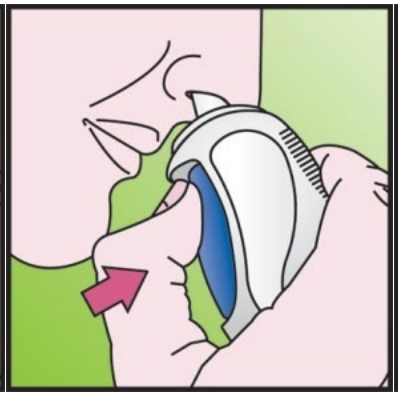


Figure 5

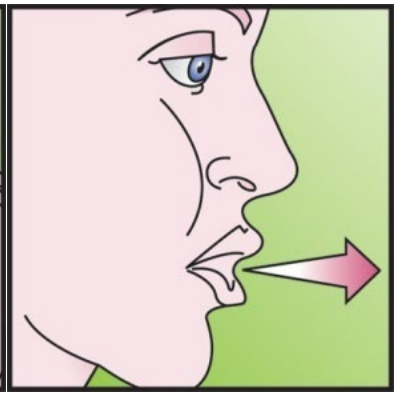


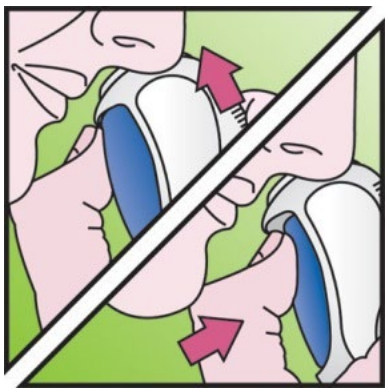
Figure 6

1. PLACE

Tilt your head forward a little bit. Hold the device upright. PLACE the nozzle in one of your nostrils (Figure 4).
Point the end of the nozzle toward the side of your nose, away from the center of your nose (septum). This helps get the medicine to the right part of your nose.

2. PRESS

PRESS the button all the way in 1 time to spray the medicine in your nose while you are breathing in (Figure 5).
Do not get any spray in your eyes. If you do, rinse your eyes well with water.
Take the nozzle out of your nose. Breathe out through your mouth (Figure 6).



3. REPEAT

To deliver the medicine to the other nostril, REPEAT Steps 1 and 2 in the other nostril (Figure 7).
If your healthcare provider has told you to take 2 sprays in each nostril, do Steps 1-3 again.
Put the cap back on the device after you have finished taking your dose.

How to clean your *AVAMYS NASAL SPRAY*

Figure 8

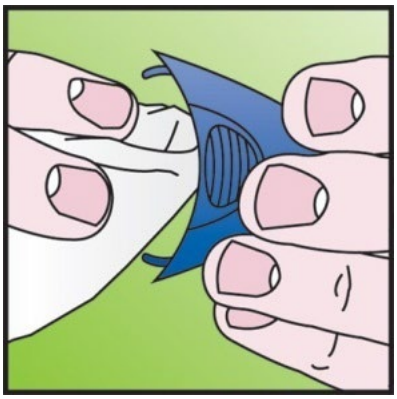


Figure 9

After each use: wipe the nozzle with a clean, dry tissue (Figure 8). Never try to clean the nozzle with a pin or anything sharp because this will damage the nozzle. Do not use water to clean the nozzle.
Once a week: clean the inside of the cap with a clean, dry tissue (Figure 9). This will help keep the nozzle from getting blocked.

How to store your *AVAMYS NASAL SPRAY*

- Keep your *AVAMYS NASAL SPRAY* and all medicines out of the reach of children.
- Store below 30°C). Do not refrigerate or freeze.
- Store with the cap on.
- Store in an upright position.

10. DETAILS OF MANUFACTURER

Manufactured by:

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

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited
Registered Office:
Dr. Annie Besant Road, Worli,
Mumbai 400 030 India.

11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Import-279/2011 dated 9th August 2011

12. DATED OF REVISION

28th July 2021

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Version AVM/PI/IN/ARD/2021/02

Adapted from GDS 11 / IPI 10 Fluticasone furoate (Intranasal formulation) dated 03 April 2018