AVAMYS NASAL SPRAY
Fluticasone furoate

QUALITATIVE AND QUANTITATIVE COMPOSITION
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.

PHARMACEUTICAL FORM
Nasal spray, suspension.

CLINICAL PARTICULARS
Indications
AVAMYS is indicated for the treatment of the symptoms of allergic rhinitis in patients 2 years of age and older.

Dosage and 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, and the patient should be informed that their symptoms will improve with continuous regular use. The duration of treatment should be restricted to the period that corresponds to allergenic exposure.

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

Children (2-11 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 allergic rhinitis in children under 2 years of age.

Elderly
No dosage adjustment required (*see Pharmacokinetics*).

Renal impairment
No dosage adjustment required (*see Pharmacokinetics*).

Hepatic impairment
No dosage adjustment is required in patients with hepatic impairment (*see Warnings and Precautions, and Pharmacokinetics*).

Contraindications
AVAMYS Nasal Spray is contraindicated in patients with hypersensitivity to any of the ingredients.

Warnings and Precautions
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 Interactions and Pharmacokinetics*).

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 Adverse Reactions and Clinical Studies*). Therefore, children should be maintained on the lowest dose which delivers adequate symptom control (*see Dosage and Administration*). As with other intranasal corticosteroids, physicians should be alert to potential systemic steroid effects including ocular changes such as central serous chorioretinopathy (*see Clinical Studies*).

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.

In addition, consideration should be given to referring the patient to a paediatric specialist. 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.

Nasal and inhaled corticosteroids may result in the development of glaucoma and/or cataracts. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma and/or cataracts.

AVAMYS Nasal Spray contains benzalkonium chloride. It may cause irritation of the nasal mucosa.

Interactions
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 hours 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 Warnings and Precautions, and Pharmacokinetics*).

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 Pre-Clinical Safety Data, 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 Pre-Clinical Safety Data, Reproductive Toxicology*).

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

Administration of fluticasone furoate to women who are breastfeeding should only be considered if the expected benefit to the mother is greater than any possible risk to the child.

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.

Adverse Reactions
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

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

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 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

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 Pharmacokinetics*).

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

PHARMACOLOGICAL PROPERTIES
Mechanism of Action
Fluticasone furoate is a synthetic trifluorinated corticosteroid that possesses a very high affinity for the glucocorticoid receptor and has a potent antiinflammatory action.

Pharmacokinetics
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 (2,640 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 $AUC_{(0-\infty)}$ (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 pharmacokinetic
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.

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 ±5 mmHg 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].

Pre-Clinical Safety Data
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.

Animal toxicology and/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.

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

Incompatibilities
None.

Shelf Life
The expiry date is indicated on the packaging.

Special Precautions for Storage
Store below 30°C.

Do not refrigerate or freeze.

In-use shelf life: 2 months.

Nature and Contents of Container
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 120 sprays after priming.

Not all presentations are available in every country.

Instructions for Use/Handling
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

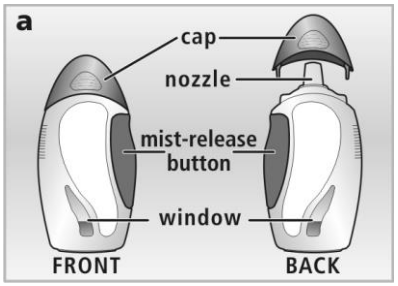
Spray is a thick suspension that becomes liquid when vigorously shaken. It will only spray when it becomes liquid. The patient must then press the button firmly all the way in, approximately 6 times until a fine mist is seen (to ensure a full dose is delivered). Once primed, the patient must shake the 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**

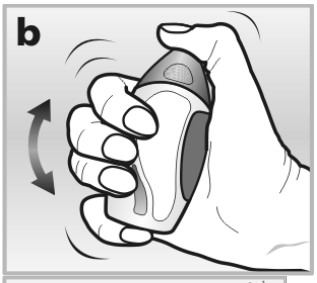
The nasal spray

- Your medicine comes in a brown glass bottle inside a plastic casing. It will contain 120 sprays **(picture a)**.
- A window in the plastic casing allows you to see how much medicine is left. You will not be able to see the liquid level 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.

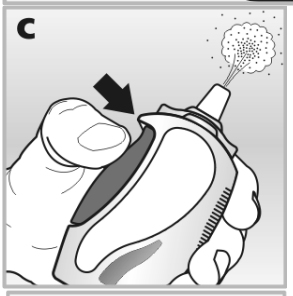


Six important things you need to know about AVAMYS Nasal Spray

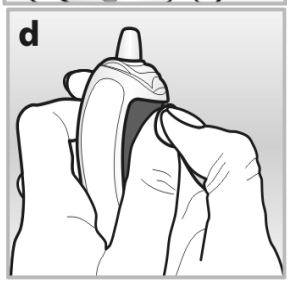
1. The nasal spray comes in a brown glass bottle. To check how much is left, **hold the nasal spray upright against a bright light**. You will then be able to see the level through the window.
2. When you **first use the nasal spray** you must **shake it vigorously** with the cap on for about 10 seconds. 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.



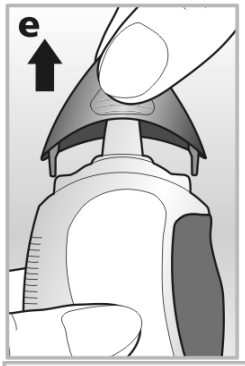
Preparing the nasal spray

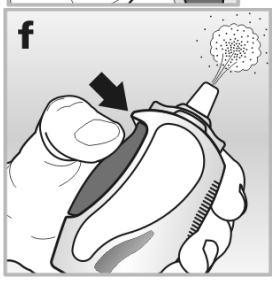
You must prepare the nasal spray:

- 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:

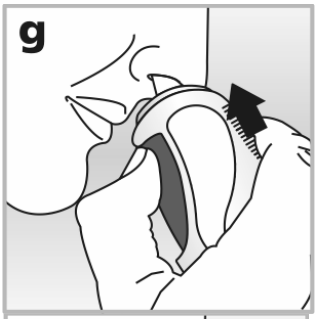
- With the cap on, **shake the nasal spray vigorously** for about 10 seconds.
- Remove the cap by gently squeezing the sides of the cap with your thumb and forefinger and pulling it straight off **(picture e)**.
- Hold the nasal spray upright and point the nozzle away from you.
- **Press the button firmly 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.

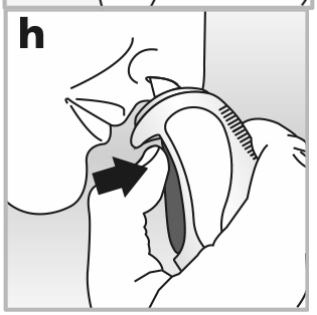




Using the nasal spray

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.





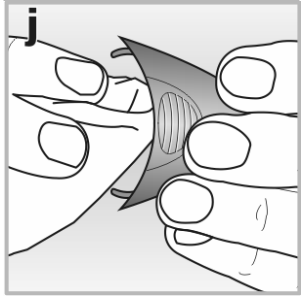
Cleaning the nasal spray

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, return it to your pharmacist.



Package Quantities and Registration Number
Box, bottle contains 120 sprays, Reg. No. DKI2191601556A1

HARUS DENGAN RESEP DOKTER

Manufactured by
Glaxo Wellcome S.A.
Aranda, Spain

Imported by
PT Glaxo Wellcome Indonesia
Jakarta, Indonesia

Version number: GDS11/IPI10 *(Extend Indication Children)*
Date of issue: 03 April 2018

INFORMASI UNTUK PASIEN

AVAMYS *NASAL SPRAY*
Fluticasone furoate

Baca keseluruhan brosur ini secara teliti sebelum Anda mulai menggunakan AVAMYS *Nasal Spray* karena brosur ini mengandung informasi penting untuk Anda.
- Simpan petunjuk ini. Anda mungkin membutuhkannya untuk dibaca kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat.
- AVAMYS *Nasal Spray* ini hanya diresepkan kepada Anda. Jangan diberikan kepada orang lain. Hal tersebut dapat membahayakan mereka, meskipun gejala penyakit mereka sama dengan gejala Anda.
- Jika Anda merasakan efek samping, bicarakan dengan dokter, apoteker, atau perawat. Termasuk kemungkinan efek samping lain yang tidak tertulis dalam petunjuk ini. Lihat *Bagian 4*.

Apa saja yang ada dalam petunjuk ini:

1 Apa itu AVAMYS *Nasal Spray* dan digunakan untuk apa

AVAMYS *Nasal Spray* (fluticasone furoate) termasuk dalam golongan obat yang disebut kortikosteroid. AVAMYS *Nasal Spray* berguna untuk mengurangi inflamasi yang disebabkan oleh alergi (rinitis) dan juga mengurangi gejala alergi.

AVAMYS *Nasal Spray* digunakan untuk meredakan gejala dari rinitis alergi termasuk hidung tersumbat, hidung meler atau gatal, bersin, dan mata berair, merah atau gatal, pada orang dewasa dan anak usia 2 tahun ke atas.

Gejala alergi dapat terjadi pada waktu tertentu tiap tahunnya dan dapat disebabkan oleh alergi terhadap serbuk sari tumbuhan (*hay fever*), atau alergi sepanjang tahun yang disebabkan oleh alergi terhadap bulu/rambut hewan, tungau debu rumah atau jamur dan terhadap penyebab alergi umum lainnya.

2 Apa yang perlu Anda ketahui sebelum menggunakan AVAMYS *Nasal Spray*

Jangan gunakan AVAMYS *Nasal Spray*:
Jika Anda alergi terhadap fluticasone furoate atau bahan lain dari AVAMYS *Nasal Spray* (terdaftar di *Bagian 6*).

Peringatan dan Perhatian
Anak-anak dan Remaja
Jangan gunakan pada anak di bawah 2 tahun.

Penggunaan AVAMYS *Nasal Spray*:
- Jika digunakan dalam jangka panjang dapat menyebabkan pertumbuhan anak menjadi lebih lambat. Dokter akan memeriksa tinggi badan anak Anda secara rutin, dan memastikan bahwa anak Anda telah menggunakan dosis efektif serendah mungkin.
- Dapat menyebabkan kondisi tertentu pada mata seperti glaukoma (meningkatnya tekanan pada mata) atau katarak (lensa mata berkabut). Sampaikan pada dokter jika Anda pernah mengalami gejala tersebut sebelumnya, atau jika Anda merasa penglihatan kabur atau mengalami gangguan penglihatan seperti *central serous chorioretinopathy* selama penggunaan AVAMYS *Nasal Spray*.

Obat Lain dan AVAMYS *Nasal Spray*
Beritahukan dokter atau apoteker jika Anda sedang, baru saja, atau akan menggunakan obat lain, termasuk obat yang didapat tanpa resep dokter. Sangat penting untuk menyampaikan kepada dokter bahwa Anda sedang, baru saja, atau akan menggunakan obat-obat berikut:
- tablet atau injeksi steroid,

- krim steroid,
- obat-obatan untuk **asma**,
- ritonavir atau cobicistat, yang digunakan dalam terapi **HIV**,
- ketoconazole, yang digunakan dalam **infeksi yang disebabkan jamur**.

Dokter akan menilai apakah Anda boleh menggunakan AVAMYS *Nasal Spray* bersama obat-obatan di atas. Dokter akan mengawasi jika Anda sedang menggunakan obat-obatan di atas karena dapat meningkatkan efek samping AVAMYS *Nasal Spray*.

AVAMYS *Nasal Spray* sebaiknya tidak digunakan bersamaan dengan *nasal spray* yang mengandung steroid lainnya.

Kehamilan dan Menyusui
Jika Anda sedang hamil atau menyusui, merasa mungkin hamil, atau berencana untuk memiliki anak, tanyakan saran kepada dokter sebelum menggunakan AVAMYS *Nasal Spray*.

Jangan gunakan AVAMYS *Nasal Spray* apabila Anda sedang hamil, atau berencana untuk hamil, kecuali atas saran/petunjuk dokter atau apoteker.

Jangan gunakan AVAMYS *Nasal Spray* apabila Anda sedang menyusui kecuali atas saran/petunjuk dokter atau apoteker.

Berkendara dan Menjalankan Mesin
AVAMYS *Nasal Spray* cenderung tidak mempengaruhi kemampuan Anda mengemudi atau menjalankan mesin.

AVAMYS *Nasal Spray* Mengandung Benzalkonium Chloride
Pada beberapa pasien, benzalkonium chloride dapat menyebabkan iritasi hidung. Beritahukan dokter atau apoteker jika Anda merasa tidak nyaman ketika menggunakan alat *spray*.

3 Bagaimana cara menggunakan AVAMYS *Nasal Spray*

Selalu gunakan obat sesuai petunjuk dokter atau apoteker. Jangan melebihi dosis yang disarankan. Pastikan dengan dokter atau apoteker apabila Anda tidak yakin.

Kapan Menggunakan AVAMYS *Nasal Spray*
- Gunakan satu kali sehari.
- Gunakan pada waktu yang sama tiap harinya.

Hal ini akan meredakan gejala Anda baik siang maupun malam hari.

Berapa Lama Waktu yang Dibutuhkan AVAMYS *Nasal Spray* untuk Mulai Bekerja
Beberapa orang tidak akan merasakan efek sepenuhnya hingga beberapa hari setelah penggunaan AVAMYS *Nasal Spray* yang pertama. Namun, biasanya AVAMYS *Nasal Spray* dapat bekerja secara efektif dalam 8 hingga 24 jam setelah penggunaan.

Seberapa Banyak Obat Digunakan
Dewasa dan Anak-anak Usia 12 Tahun dan Lebih
- **Dosis awal** adalah 2 semprot pada tiap lubang hidung satu kali sehari.
- Ketika gejala sudah terkontrol, Anda dapat mengurangi dosis menjadi 1 semprot pada tiap lubang hidung satu kali sehari.

Anak-anak Usia 2 Sampai 11 Tahun
- **Dosis awal** adalah 1 semprot pada tiap lubang hidung satu kali sehari.
- Jika gejala bertambah buruk, maka dokter dapat meningkatkan dosis menjadi 2 semprot pada tiap lubang hidung satu kali sehari hingga gejala dapat terkontrol. Kemudian setelah gejala terkontrol, dosis dapat dikurangi menjadi 1 semprot pada tiap lubang hidung satu kali sehari.

Anak-anak Usia di Bawah 2 Tahun
Tidak ada data penggunaan pada anak usia di bawah 2 tahun. Keamanan dan efikasi pada kelompok ini masih belum jelas.

Bagaimana Cara Menggunakan *Nasal Spray*

AVAMYS *Nasal Spray* sebenarnya tidak memiliki rasa maupun bau. Obat ini disemprotkan ke dalam hidung dalam bentuk kabut halus. Hati-hati agar mata tidak terkena semprotan. Jika terkena mata, segera cuci mata Anda dengan air.

Terdapat langkah-langkah petunjuk menggunakan *nasal spray* pada *Bagian 7* leaflet ini. Ikuti petunjuk dengan benar untuk mendapatkan manfaat penuh dari AVAMYS *Nasal Spray*.

Lihat langkah-langkah petunjuk penggunaan *nasal spray*, pada *Bagian 7*

Jika Anda Menggunakan AVAMYS *Nasal Spray* Lebih dari yang Seharusnya
Konsultasikan kepada dokter atau apoteker.

Jika Anda Lupa untuk Menggunakan AVAMYS *Nasal Spray*
Jika Anda melewatkan satu dosis, segera gunakan AVAMYS *Nasal Spray* tepat saat Anda ingat.

Jika waktu Anda ingat sudah mendekati waktu untuk penggunaan dosis selanjutnya, maka tunggu hingga penggunaan dosis selanjutnya tersebut. Jangan gunakan dosis ganda untuk menggantikan dosis yang terlewatkan.

Jika Anda memiliki pertanyaan lebih lanjut terkait penggunaan obat ini, atau Anda merasa tidak nyaman saat menggunakan *nasal spray* tanyakan kepada dokter, apoteker, atau perawat.

4 Efek samping yang mungkin terjadi

Seperti obat lainnya, obat ini dapat menyebabkan efek samping, meski tidak semua pasien mengalaminya.

Reaksi Alergi: Segera Cari Pertolongan Dokter
Reaksi alergi pada AVAMYS *Nasal Spray* jarang dan terjadi pada kurang dari 1 dalam 1.000 pasien. Dalam jumlah kecil, reaksi alergi dapat menjadi hal yang serius dan bahkan dapat mengancam jiwa seseorang jika tidak cepat ditangani. Gejala yang terjadi termasuk:
- merasa sangat kedinginan, batuk atau kesulitan bernapas,
- mendadak merasa lemah atau kepala terasa ringan (yang dapat mengakibatkan roboh atau hilang kesadaran),
- bengkak di area wajah,
- ruam pada kulit atau kemerahan.

Pada banyak kasus, gejala ini dapat dianggap menjadi efek samping yang tidak terlalu serius. **Namun Anda harus tetap waspada bahwa gejala ini juga berpotensi menjadi efek samping yang serius,** jadi jika Anda merasakan gejala ini: **Hubungi dokter sesegera mungkin.**

Efek Samping yang Sangat Umum Terjadi
Hal ini mungkin dapat terjadi pada **≥1/10** pasien:
- Hidung berdarah (umumnya minor), terutama jika Anda menggunakan AVAMYS *Nasal Spray* selama lebih dari 6 minggu berturut-turut.

Efek Samping yang Umum Terjadi
Hal ini mungkin dapat terjadi pada **≥1/100** hingga **<1/10** pasien:
- Luka pada hidung, yang dapat menyebabkan iritasi atau hidung menjadi tidak nyaman. Anda mungkin dapat mengalami lecet juga ketika Anda menghembuskan napas (dengan kencang) dari hidung.
- Sakit kepala.

Efek Samping yang Tidak Umum Terjadi
Hal ini mungkin dapat terjadi pada **≥1/1.000** hingga **<1/100** pasien:
- Nyeri, rasa terbakar, iritasi, rasa sakit dan kering pada hidung.

Efek Samping yang Jarang Terjadi
Hal ini mungkin dapat terjadi pada **≥1/10.000** dan **<1/1.000** pasien:
- Reaksi alergi termasuk anafilaksis, bengkak pada wajah, ruam dan gatal-gatal.

Efek Samping yang Sangat Jarang Terjadi
Hal ini mungkin dapat terjadi pada **<1/10.000** pasien:
- Robekan kecil pada punggung bagian dalam hidung yang memisahkan dua lubang hidung.

Efek Samping yang Tidak Diketahui

Frekuensi tidak dapat diperkirakan dari data yang tersedia:
- Kecepatan pertumbuhan yang menurun pada anak-anak.

Nasal kortikosteroid dapat mempengaruhi produksi hormon pada tubuh Anda, terutama jika digunakan dengan dosis tinggi dalam jangka waktu yang lama. Pada anak-anak efek samping ini dapat menyebabkan pertumbuhan mereka melambat dibanding pada anak lainnya.

Pelaporan Kejadian Tidak Diinginkan
Jika Anda merasakan kejadian tidak diinginkan, laporkan ke dokter, apoteker, atau perawat. Termasuk kemungkinan kejadian tidak diinginkan lain yang tidak tertulis dalam brosur ini.

5 Bagaimana cara penyimpanan AVAMYS *Nasal Spray*

Simpan obat ini jauh dari jangkauan anak-anak.

Penyimpanan AVAMYS *Nasal Spray* terbaik adalah dengan posisi berdiri tegak. Pastikan kemasan selalu tertutup.

Jangan gunakan obat setelah tanggal kedaluwarsa yang tertulis pada kemasan label dan karton. Tanggal kedaluwarsa merujuk pada hari terakhir bulan tersebut. AVAMYS *Nasal Spray* sebaiknya digunakan dalam waktu 2 bulan setelah kemasan pertama kali dibuka.

Jangan didinginkan atau dibekukan.

Jangan membuang obat apapun di air limbah atau limbah rumah tangga. Tanyakan pada apoteker bagaimana cara membuang obat yang tidak digunakan lagi. Langkah ini membantu dalam menjaga lingkungan.

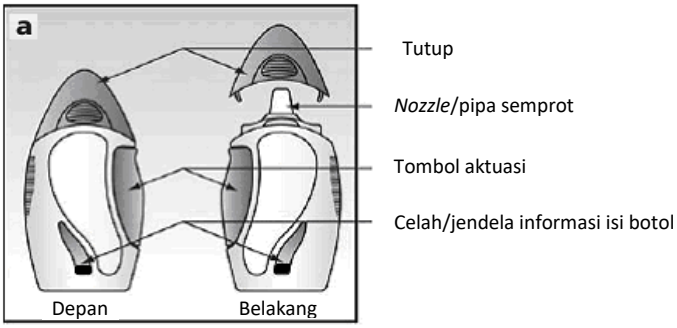
6 Isi dari kemasan dan informasi lain

Kandungan AVAMYS *Nasal Spray*
Zat aktif AVAMYS *Nasal Spray* adalah fluticasone furoate. Setiap semprotan mengandung 27,5 mikrogram fluticasone furoate. Bahan lainnya adalah glucose anhydrous, dispersible cellulose, polysorbate 80, benzalkonium chloride, disodium edetate, air murni (Lihat *Bagian 2*).

Seperti Apa Bentuk AVAMYS *Nasal Spray* dan Isi dari Kemasan
AVAMYS *Nasal Spray* adalah suspensi *nasal spray* dalam botol kaca coklat, dilengkapi dengan pompa semprot. Botol berada dalam bungkus plastik berwarna putih dengan tutup berwarna biru muda dan tombol aktuasi samping. Bungkus plastik memiliki celah/jendela yang dapat menunjukkan isi botol.

7 Cara pakai

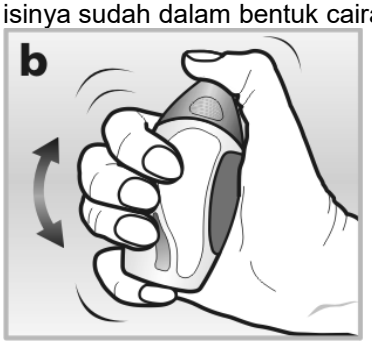
Seperti Apakah *Nasal Spray* Itu?
Nasal spray dikemas dalam botol kaca coklat dalam bungkus plastik – lihat **Gambar a**.



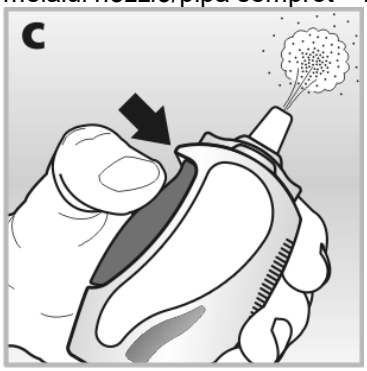
Celah/jendela pada bungkus plastik membuat Anda dapat mengetahui berapa banyak AVAMYS *Nasal Spray* yang tersisa dalam botol.

Enam Hal Penting yang Harus Anda Ketahui Tentang Cara Penggunaan *Nasal Spray*
- AVAMYS *Nasal Spray* dikemas dalam botol kaca berwarna coklat. Jika Anda ingin mengetahui sisa obat dalam botol, maka **peganglah *nasal spray* dengan posisi tegak lurus di bawah sinar terang**. Anda dapat melihat permukaan cairan melalui celah/jendela pada bungkus.
- Pada **penggunaan *nasal spray* yang pertama**, Anda perlu **mengocok kemasan dengan kuat** dengan tutup tetap terpasang selama kurang lebih 10 detik. Hal ini penting dilakukan karena AVAMYS *Nasal Spray* adalah suspensi kental yang akan menjadi cair ketika Anda mengocoknya

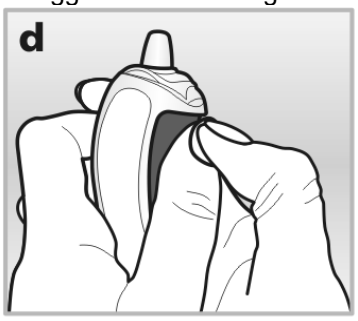
dengan sempurna – lihat **Gambar b**. AVAMYS *Nasal Spray* hanya dapat disemprotkan apabila isinya sudah dalam bentuk cairan.



- Tombol aktuasi harus **ditekan dengan kuat hingga masuk ke dalam**, untuk mengeluarkan obat melalui *nozzle*/pipa semprot – lihat **Gambar c**.



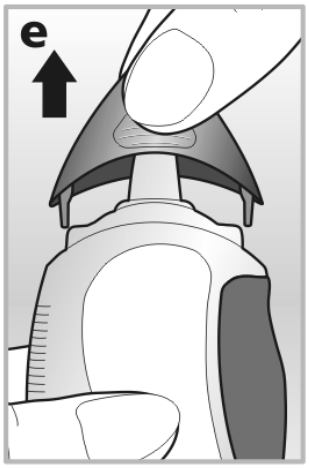
- Jika Anda mengalami kesulitan saat menekan tombol aktuasi dengan ibu jari, Anda dapat menggunakan dua tangan – lihat **Gambar d**.



- **Pastikan kemasan selalu tertutup rapat** ketika tidak digunakan. Menutup kemasan dapat menghindarkan obat dari debu, menjaga tekanan dan mencegah *nozzle*/pipa semprot tersumbat. Ketika kemasan dalam kondisi tertutup, tombol aktuasi tidak dapat ditekan.
- **Jangan pernah gunakan jarum** atau benda tajam lain untuk membersihkan *nozzle*/pipa semprot. Hal ini akan merusak *nasal spray*.

Mempersiapkan *Nasal Spray* untuk Digunakan
Anda Harus Mempersiapkan *Nasal Spray*:
- Sebelum Anda menggunakan AVAMYS *Nasal Spray* untuk pertama kali.
- Jika Anda telah meninggalkan kemasan dalam kondisi terbuka selama 5 hari atau alat tidak digunakan kembali selama 30 hari atau lebih.

Mempersiapkan *nasal spray* dapat membantu Anda agar selalu mendapatkan dosis penuh dari obat. Ikuti langkah-langkah berikut:
1. **Kocok *nasal spray* dengan kuat** dengan tutup tetap terpasang selama kurang lebih 10 detik.
2. Lepaskan tutup dengan menarik bagian tutup menggunakan ibu jari dan jari telunjuk – lihat **Gambar e**.

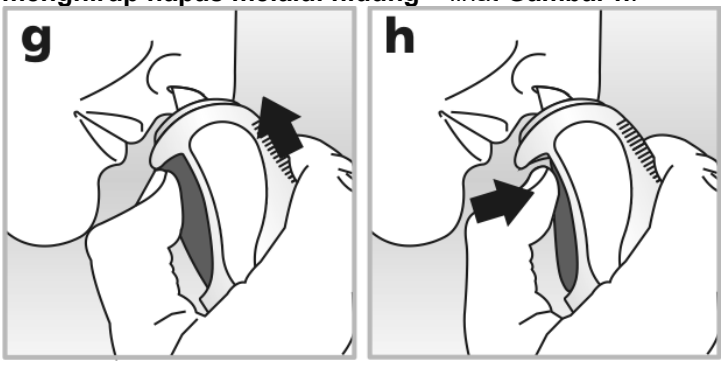


3. Pegang *nasal spray* dengan posisi tegak lurus, kemudian miringkan dan **arahkan *nozzle*/pipa semprot menjauh dari Anda**.
4. **Tekan tombol aktuasi dengan kuat** hingga masuk ke dalam. **Lakukan langkah ini setidaknya 6 kali** hingga alat dapat mengeluarkan kabut halus ke udara – lihat **Gambar f**.

***Nasal spray* sudah siap untuk digunakan**.

Menggunakan *Nasal Spray*

1. **Kocok *nasal spray*** dengan kuat.
2. **Lepaskan tutup wadah**.
3. **Hembuskan napas** agak kencang untuk membersihkan lubang hidung Anda, kemudian miringkan kepala Anda agak ke depan.
4. Letakkan *nozzle*/pipa semprot di salah satu lubang hidung Anda – lihat **Gambar g**. Arahkan ujung *nozzle*/pipa semprot agak ke dinding luar hidung, menjauhi bagian tengah hidung. Hal ini akan membantu obat mengarah ke bagian yang tepat dalam hidung.
5. **Tekan tombol aktuasi dengan kuat** hingga masuk ke dalam, **bersamaan dengan Anda menghirup napas melalui hidung** – lihat **Gambar h**.



6. Keluarkan *nozzle*/pipa semprot dan **hembuskan napas melalui mulut**.
7. Jika dosis Anda adalah 2 semprot pada tiap lubang hidung maka ulangi langkah 4 hingga 6.
8. Ulangi langkah 4 hingga 7 pada lubang hidung lainnya.
9. **Tutup kemasan** kembali dengan rapat.

Membersihkan *Nasal Spray*

Setiap Setelah Penggunaan:

1. Usap *nozzle*/pipa semprot dan tutup kemasan bagian dalam dengan tisu bersih dan kering – lihat **Gambar i dan j**.

2. Jangan gunakan air untuk membersihkan alat.
3. **Jangan pernah gunakan jarum** atau benda tajam lain untuk membersihkan *nozzle*/pipa semprot.
4. **Selalu tutup kemasan kembali** setelah selesai penggunaan.

Jika *Nasal Spray* Tidak Dapat Bekerja dengan Semestinya:

1. Periksa apakah masih ada obat yang tersisa. Lihat permukaan cairan melalui celah/jendela kemasan. Jika cairan tampak sangat sedikit maka ada kemungkinan obat yang tersisa tidak cukup untuk dikeluarkan kembali.
2. Periksa alat apabila kemungkinan terdapat kerusakan.
3. Jika Anda merasa *nozzle*/pipa semprot tersumbat, **jangan gunakan jarum** atau benda tajam lain untuk membersihkannya.
4. Coba atur kembali alat dengan mengikuti petunjuk bagian *"Mempersiapkan Nasal Spray untuk Digunakan"*.
5. Jika alat masih tidak dapat bekerja dengan semestinya, atau hanya mengeluarkan cairan, bawa alat kembali kepada apoteker untuk mendapatkan saran.

HARUS DENGAN RESEP DOKTER

AVAMYS *Nasal Spray* 27,5 mikrogram
Dus, 1 botol @ 120 *spray* Reg. No. DKI2191601556A1

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