PACKAGE INSERT

AZELASTINE HYDROCHLORIDE
FLUTICASONE PROPIONATE

Dymista®

137 micrograms / 50 micrograms per actuation
Anti-allergy – Corticosteroid Combination

Nasal Suspension (Spray)

PHARMACOLOGIC CATEGORY

Anti-allergic – Corticosteroid Combination

PRODUCT DESCRIPTION

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is a white, homogenous suspension.
Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray contains two active substances: azelastine hydrochloride and fluticasone propionate.

FORMULATION/COMPOSITION

Each g of suspension contains 1 mg Azelastine Hydrochloride, EP and 365 mcg Fluticasone Proprionate, EP.
Each actuation (140 mg) delivers 137 micrograms Azelastine Hydrochloride, EP (equivalent to 125 micrograms azelastine) and 50 micrograms Fluticasone Proprionate, EP.

List of excipients
Disodium edetate, Glycerol, Microcrystalline cellulose, Carmellose sodium, Polysorbate 80, Benzalkonium chloride, Phenylethyl alcohol, Purified water.

PHARMACODYNAMICS AND PHARMACOKINETICS

Mechanism of action and phaincodynamic effects
Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray contains azelastine hydrochloride and fluticasone propionate, which have different modes of action and show synergistic effects in terms of improvement of allergic rhinitis and rhino-conjunctivitis symptoms.

Fluticasone propionate
Fluticasone propionate is a synthetic trifluorinated corticosteroid that possesses a very high affinity for the glucocorticoid receptor and has a potent anti-inflammatory action, e.g. 3-5 fold more potent than dexamethasone in cloned human glucocorticoid receptor binding and gene expression assays.

Azelastine hydrochloride
Azelastine, a phthalazinone derivative is classified as a potent long-acting anti-allergic compound with selective H_1-antagonist, mast cell stabilizing and anti-inflammatory properties. Data from *in vivo* (preclinical) and *in vitro* studies show that azelastine inhibits the synthesis or release of the chemical mediators known to be involved in early and late stage allergic reactions, e.g. leukotrienes, histamine, platelet-activating factor (PAF) and serotonin.
A relief of nasal allergic symptoms is observed within 15 minutes after administration.

Azelastine hydrochloride + fluticasone propionate (Dymista) Nasal Spray
In 4 clinical studies in adults and adolescents with allergic rhinitis, one spray of Azelastine hydrochloride + Fluticasone propionate (Dymista) in each nostril twice daily significantly improved nasal symptoms (comprising rhinorrhoea, nasal congestion, sneezing and nasal itching) compared with placebo, azelastine hydrochloride alone and fluticasone propionate alone. It significantly improved ocular symptoms (comprising itching, tearing/watering and redness of the eyes) and the patients' disease-related quality of life (Rhinoconjunctivitis Quality of Life Questionnaire – RQLQ) in all 4 studies.

In comparison to a marketed fluticasone propionate nasal spray substantial symptom improvement (50% reduction in nasal symptoms severity) was achieved significantly earlier (3 days and more) with Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray. The superior effect of Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray to fluticasone propionate nasal spray was maintained throughout one-year study in patients with chronic persistent allergic rhinitis and nonallergic/vasomotor rhinitis.

Pharmacokinetics

Absorption
After intranasal administration of two sprays per nostril (548 mcg of azelastine hydrochloride and 200 mcg of fluticasone propionate) of Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray, the mean (± standard deviation) peak plasma exposure (C_{max}) was 194.5 ± 74.24 pg/mL for azelastine and 10.3 ± 3.9 pg/mL for fluticasone propionate and the mean total exposure (AUC) was 4217 ± 2618 pg/mL*hr for azelastine and 97.7 ± 43.1 pg/mL*hr for fluticasone propionate. The median time to peak exposure (T_{max}) from a single dose was 0.5 hours for azelastine and 1.0 hours for fluticasone propionate.
There was no evidence of pharmacokinetic interactions between azelastine hydrochloride and fluticasone propionate.

Distribution
Fluticasone propionate has a large volume of distribution at steady-state (approximately 318 litre). Plasma protein binding is 91 %.
The volume of distribution of azelastine is high indicating distribution predominantly into the peripheral tissue. The level of protein binding is 80-90 %. Additionally, both drugs have broad therapeutic windows. Therefore, drug displacement reactions are unlikely.

Biotransformation
Fluticasone propionate is cleared rapidly from the systemic circulation, principally by hepatic metabolism to an inactive carboxylic acid metabolite, by the cytochrome P450 enzyme CYP3A4. Swallowed fluticasone propionate is also subject to extensive first pass metabolism.
Azelastine is metabolized to *N*- desmethylazelastine via various CYP isoenzymes, mainly CYP3A4, CYP2D6 and CYP2C19.

Elimination
The elimination rate of intravenous administered fluticasone propionate is linear over the 250—1000 microgram dose range and are characterised by a high plasma clearance (CL_s=1.1 l/min). Peak plasma concentrations are reduced by approximately 98% within 3-4 hours and only low plasma concentrations were associated with the 7.8 h terminal half-life. The renal clearance of fluticasone propionate is negligible (<0.2%) and less than 5% as the carboxylic acid metabolite. The major route of elimination is the excretion of fluticasone propionate and its metabolites in the bile.
Plasma elimination half-lives after a single dose of azelastine are approximately 20-25 hours for azelastine and about 45 hours for the therapeutically active metabolite N-desmethylazelastine. Excretion occurs mainly via the faeces. The sustained excretion of small amounts of the dose in the faeces suggests that some enterohepatic circulation may take place.

INDICATIONS

Indication: Symptomatic treatment of moderate to severe allergic rhinitis and rhino-conjunctivitis in adults and children 6 years and older where use of a combination (intranasal antihistamine and glucocorticoid) is appropriate
Target Population: Adults and adolescents (6 years and above)

DOSAGE AND MODE/ROUTE OF ADMINISTRATION

Posology
For full therapeutic benefit regular usage is essential.
Contact with the eyes should be avoided.

Adults and children (6 years and above)
One actuation in each nostril twice daily (morning and evening).

Children below 6 years
Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is not recommended for use in children below 6 years of age as safety and efficacy has not been established in this age group.

Elderly
No dose adjustment is required in this population.

Renal and hepatic impairment
There are no data in patients with renal and hepatic impairment.

Duration of treatment
Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is suitable for long-term use.

Method of administration
Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is for nasal use only.

Instruction for use
Preparing the spray:
The bottle should be shaken gently before use for about 5 seconds by tilting it upwards and downwards and the protective cap be removed afterwards. Prior to first use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray must be primed by pressing down and releasing the pump 6 times. If Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray has not been used for more than 7 days it must be reprimed once by pressing down and releasing the pump.

Using the spray:
The bottle should be shaken gently before use for about 5 seconds by tilting it upwards and downwards and the protective cap be removed afterwards. After blowing the nose the suspension is to be sprayed once into each nostril keeping the head tilted downward (see figure). After use the spray tip is to be wiped and the protective cap to be replaced.

CONTRAINDICATIONS, PRECAUTIONS, WARNINGS

Contraindications
Hypersensitivity to the active substances or to any of the excipients.

Warnings and precautions
During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects.

Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray undergoes extensive first-pass metabolism, therefore the systemic exposure of intranasal fluticasone propionate in patients with severe liver disease is likely to be increased. The may result in a higher frequency of systemic adverse events. Caution is advised when treating these patients.

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.

In general, the dose of intranasal fluticasone formulations should be reduced to the lowest dose at which effective control of the symptoms of rhinitis is maintained. Higher doses than the recommended one have not been tested for Azelastine hydrochloride + Fluticasone propionate (Dymista). As with all intranasal corticosteroids, the total systemic burden of corticosteroids should be considered whenever other forms of corticosteroid treatment are prescribed concurrently.

Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses. Since growing up is also given in adolescents it is recommended that the growth of adolescents receiving prolonged treatment with nasal corticosteroids is regularly monitored, too. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid if possible, to the lowest dose at which effective control of symptoms is maintained.

- Azelastine hydrochloride belongs to a group of medicines called antihistamines. Antihistamines work by preventing the effects of substances such as histamine that the body produces as part of an allergic reaction – thus reducing symptoms of allergic rhinitis.
- Fluticasone propionate belongs to a group of medicines called corticosteroids which reduces inflammation.

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is used for the symptomatic treatment of moderate to severe allergic rhinitis and rhino-conjunctivitis in adults and children 6 years and older where use of a combination (intranasal antihistamine and glucocorticoid) is appropriate.

Target population: Adults and adolescents (6 years and above)

Allergic rhinitis are allergic reactions to substances such as pollen (hayfever), house mites, moulds, dust or pets.

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray relieves the symptoms of allergies, for example: runny nose, post nasal drip, sneezing and itchy or blocked nose.

2. What you need to know before you use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray

Do not use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray:
- If you are allergic to azelastine hydrochloride or fluticasone propionate or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before using Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray if:
- You had a recent operation on your nose.
- You have an infection in your nose. Infections of the nasal airways should be treated with antibacterial or antifungal medication. If you are given medication for an infection in your nose you can continue to use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray to treat your allergies.
- You have tuberculosis or an untreated infection.
- You have a change in vision or a history of increased ocular pressure, glaucoma and/or cataracts. If this applies to you, you will be closely monitored whilst using Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray.
- You suffer from impaired adrenal function. Care must be taken when transferring from systemic steroid treatment to Dymista Nasal Spray.
- You suffer from a severe liver disease. Your risk of suffering from systemic side effects is increased.

In these cases your doctor will decide whether you can use Dymista Nasal Spray.

It is important that you take your dose as instructed by your doctor or as advised by your doctor. Treatment with higher than recommended doses of nasal corticosteroids may result in adrenal suppression, a condition that may produce weight loss, fatigue, muscle weakness, low blood sugar, salt cravings, joint pains, depression and darkening of the skin. If this happens and you are worried, contact your doctor.

To avoid adrenal suppression your doctor will advise you to take the lowest dose at which effective control of your symptoms of rhinitis is maintained.

Taking nasal corticosteroids (such as Dymista) may when taken for a long time cause children and adolescents to grow more slowly. The doctor will check your child's height regularly, and make sure he or she is taking the lowest possible effective dose.

Contact your doctor, if you experience blurred vision or other visual disturbances.

If you are unsure whether the above applies to you, talk to your doctor or pharmacist before using Dymista Nasal Spray.

Children
This medicine is not recommended for children under 6 years.

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

Some medicines may increase the effects of Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat and medicines for the treatment of fungal infections: ketoconazole).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray.

Driving and using machines
Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray has minor influence on the ability to drive and use machines.
Very rarely, you may experience fatigue or dizziness due to the disease itself or when using Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray. In these cases, do not drive or operate machinery. Please be aware that drinking alcohol may enhance these effects.

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray contains benzalkonium chloride
This medicine contains 14 micrograms benzalkonium chloride in each spray, which is equivalent to 14 mcg / 140 mg. Benzalkonium chloride may cause irritation or swelling inside the nose, especially if used for a long time. Tell your doctor or pharmacist if you feel discomfort when using the spray.

3. How to use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray

Always use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray exactly as your doctor has told you. Check with your doctor or pharmacist, if you are not sure.

It is essential to use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray regularly to gain the full therapeutic benefit.

Contact with the eyes should be avoided.

Adults and adolescents (6 years and above)
- The recommended dose is one spray into each nostril in the morning and evening.

Use in children under 6 years
- This medicine is not recommended for children under 6 years.

Use in renal and hepatic impairment
- There are no data in patients with renal and hepatic impairment.

Method of administration
For nasal use.
Read the following instructions carefully and use only as directed.

INSTRUCTION FOR USE

Preparing the spray

Figure 1

1. Shake the bottle gently for about 5 seconds by tilting it upwards and downwards and then remove the protective cap (see figure 1).
2. The first time the nasal spray is used, you must prime the pump by squirting it into the air.
3. Prime the pump by putting two fingers on either side of the spray pump and place your thumb on the bottom of the bottle.
4. Press down and release the pump 6 times until a fine mist appears (see figure 2).

Figure 2

5. Now your pump is primed and ready to use.
6. If the nasal spray has not been used for more than 7 days, you will need to re-prime the pump once by pressing down and releasing the pump.

2709454

Dymista®
137 mcg / 50 mcg per actuation
Anti-allergy – Corticosteroid Combination
Nasal Suspension (Spray)
2799958
2709454
137 mcg / 50 mcg per actuation
Anti-allergy – Corticosteroid Combination
Nasal Suspension (Spray)

Package leaflet:
Information for the patient

AZELASTINE HYDROCHLORIDE
FLUTICASONE PROPIONATE

Dymista®

137 mcg / 50 mcg per actuation
Anti-allergy – Corticosteroid Combination

Nasal Suspension (Spray)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:
1. What Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is and what it is used for
2. What you need to know before you use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray
3. How to use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray
4. Possible side effects
5. How to store Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray
6. Contents of the pack and other information

1. What Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is and what it is used for

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray contains two active substances: azelastine hydrochloride and fluticasone propionate.

Using the spray

1. Shake the bottle gently for 5 seconds by tilting it upwards and downwards and then remove the protective cap (see figure 1).
2. Blow your nose to clear your nostrils.
3. Keep your head tilted downwards towards your toes. Do not tilt head backwards.


Figure 3

4. Hold the bottle upright and carefully insert the spray tip into one nostril.
5. Close other nostril with your finger, rapidly press down once and sniff gently at the same time (see figure 3).
6. Breathe out through your mouth.

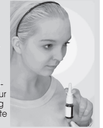
Figure 4

7. Repeat in your other nostril.
8. Breathe in gently, and do not tilt your head back after dosing. This will stop the medicine going into your throat and causing an unpleasant taste (see figure 4).
9. After each use wipe the spray tip with a clean tissue or cloth and then replace the protective cap.
10. Do not prick the nozzle in case spray is not obtained. Clean the actuator with water.

It is important that you take your dose as advised by your doctor. You should use only as much as your doctor recommends.

Duration of treatment

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is suitable for long-term use. Use this medicine for as long as your doctor tells you to.

If you use more Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray than you should

If you spray too much of this medicine into your nose you are unlikely to have any problems. If you are worried or if you have used doses higher than recommended over a long period, contact your doctor. If anyone, especially a child, accidentally drinks Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray, contact your doctor or nearest hospital casualty department as soon as possible.

If you forget to use Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray

Use your nasal spray as soon as you remember, then take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop using Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray

Do not stop using your nasal spray without asking your doctor, because this puts the success of the treatment at risk.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray can cause side effects, although not everybody gets them.

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

- Nosebleed

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

- Headache
- A bitter taste in your mouth, especially if you tilt your head backwards when you are using the nasal spray. This should go away if you have a soft drink a few minutes after using this medicine.
- Unpleasant smell

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

- Slight irritation of the inside of the nose. This can cause mild stinging, itching or sneezing.
- Nasal dryness, cough, dry throat or throat irritation

Rare side effects (These may affect up to 1 in 1,000 people):

- Dry mouth

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

- Dizziness or drowsiness
- Cataract, glaucoma or increased pressure in your eye where you may have a loss of vision and/or red and painful eyes. These side effects have been reported following prolonged treatment with fluticasone propionate nasal sprays.
- Damage of the skin and mucous membrane in the nose
- Feeling sick, weary, exhausted or weak
- Rash, itchy skin or red, raised itchy bumps
- Bronchospasm (the narrowing of the airways in the lungs)

Seek immediate medical help if you have any of the following symptoms:

- **Swelling of face, lips, tongue or throat which may cause difficulty in swallowing/ breathing and a sudden onset of skin rash.** This could be signs of a severe allergic reaction. ***Please note: This is very rare.***

Side effects with unknown frequency (frequency cannot be estimated from available data):

- Blurred vision
- Sores in the nose

Systemic side effects (side effects concerning the whole body) may occur when this medicine is used at high doses for a long time. These effects are much less likely to occur if you use a corticosteroid nasal spray than if you take corticosteroids by mouth. These effects may vary in individual patients and between different corticosteroid preparations (see section 2).

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

In rare cases a reduction of the bone density (osteoporosis) was observed, if nasal corticosteroids were administered long-term.

Reporting of side effects

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

5. How to store Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray

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

Do not use this medicine after the expiry date which is stated on the bottle label and the outer carton after "EXP". The expiry date refers to the last day of that month.

Do not refrigerate or freeze.

Store at temperatures not exceeding 30°C.

Shelf-life:

Bottle with 23 g suspension in 25 ml bottles: 24 months

Shelf life after first opening: Dispose of any unused medicine 3 months after you first open the nasal spray.

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

6. Contents of the pack and other information

What Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray contains

The active substances are: Azelastine Hydrochloride, EP and Fluticasone Propionate, EP.

Each g of suspension contains 1 mg Azelastine Hydrochloride, EP and 365 mcg Fluticasone Propionate, EP.

Each actuation (140 mg) delivers 137 mcg Azelastine Hydrochloride, EP (equivalent to 125 mcg azelastine) and 50 mcg Fluticasone Propionate, EP.

The other ingredients are: Disodium edetate, glycerol, microcrystalline cellulose, carmellose sodium, polysorbate 80, benzalkonium chloride, phenylethyl alcohol and purified water.

What Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray looks like and contents of the pack

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is a white, homogenous suspension.

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray comes in an amber coloured glass bottle fitted with a spray pump, applicator and a protective cap.

The 25 ml bottle contains 23 g nasal spray, suspension (at least 120 actuations).

Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray is presented in:

Packs containing 1 bottle with 23 g nasal spray, suspension

Marketing Authorisation Holder

Viatris Pharmaceuticals, Inc.,
22nd floor, Units C&D, Menarco Tower
32nd St. Bonifacio Global City, Taguig City,
Metro Manila

Manufactured by:

Cipla Limited, Plot No. 9 & 10, Indore Special Economic Zone, Phase II, Pithampur, District Dhar, Madhya Pradesh, IN-454 775, India

Caution:

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

Registration no.: DR-XY47527

Date of First Authorization: 10 November 2021

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Version 1.1

VIATRIS

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Close monitoring is warranted in patients with a change in vision or with a history of increased ocular pressure, glaucoma and/or cataracts.

If there is any reason to believe that adrenal function is impaired, care must be taken when transferring patients from systemic steroid treatment to Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray.

In patients who have tuberculosis, any type of untreated infection, or have had a recent surgical operation or injury to the nose or mouth, the possible benefits of the treatment with Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray should be weighed against possible risk.

Infections of the nasal airways should be treated with antibacterial or antimycotical therapy, but do not constitute a specific contraindication to treatment with Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray.

Azelastine hydrochloride + Fluticasone propionate (Dymista) contains benzalkonium chloride. Long term use may cause oedema of the nasal mucosa.

PREGNANCY AND LACTATION

Pregnancy

There are no or limited amount of data from the use of azelastine hydrochloride and fluticasone propionate in pregnant women. Therefore, Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Lactation

It is unknown whether nasally administered azelastine hydrochloride/ metabolites or fluticasone propionate/metabolites are excreted in human breast milk. Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray should be used during lactation only if the potential benefit justifies the potential risk to the newborns/infant.

INTERACTIONS

Fluticasone propionate

Under normal circumstances, low plasma concentrations of fluticasone propionate are produced after intranasal dosing, due to extensive first pass metabolism and high systemic clearance mediated by cytochrome P450 3A4 in the gut and liver. Hence, clinically significant drug interactions mediated by fluticasone propionate are unlikely.

A drug interaction study in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 inhibitor) can greatly increase fluticasone propionate plasma concentrations, resulting in markedly reduced serum cortisol concentrations. During postmarketing use, there have been reports of clinically significant drug interactions in patients receiving intranasal or inhaled fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects. Co-treatment with other CYP 3A4 inhibitors, including cobicistat-containing products is also expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

Studies have shown that other inhibitors of cytochrome P450 3A4 produce negligible (erythromycin) and minor (ketoconazole) increases in systemic exposure to fluticasone propionate without notable reductions in serum cortisol concentrations. Nevertheless, care is advised when co-administering potent cytochrome P450 3A4 inhibitors (e.g. ketoconazole), as there is potential for increased systemic exposure to fluticasone propionate.

Azelastine hydrochloride

No specific interaction studies with azelastine hydrochloride nasal spray have been performed. Interaction studies at high oral doses have been performed. However, they bear no relevance to azelastine nasal spray as given recommended nasal doses result in much lower systemic exposure. Nevertheless, care should be taken when administering azelastine hydrochloride in patients taking concurrent sedative or central nervous medications because sedative effect may be enhanced. Alcohol may also enhance this effect.

ADVERSE DRUG REACTIONS

Commonly, dysgeusia, a substance-specific unpleasant taste, may be experienced after administration (often due to incorrect method of application, namely tilting the head too far backwards during administration).

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as:

Very common	Common	Uncommon	Rare	Very rare	Not known
(≥1/10)	(≥1/100 to <1/10)	(≥1/1,000 to <1/100)	(≥1/10,000 to <1/1,000)	(<1/10,000)	(cannot be estimated from the available data)

Frequency System Organ Class	*Very common*	*Common*	*Uncommon*	*Rare*	*Very rare*	*Not known*
Immune system disorders					Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm	
Nervous system disorder		Headache, Dysgeusia, unpleasant smell			Dizziness, somnolence	
Eye disorders*					Glaucoma, increased intraocular pressure, cataract	Vision, blurred
Respiratory, thoracic and mediastinal disorders	Epistaxis		Nasal discomfort, sneezing, nasal dryness, cough, dry throat, throat irritation		Nasal septal perforation**, mucosal erosion	Nasal ulcers
Gastrointestinal disorders				Dry mouth	Nausea	
Skin and subcutaneous tissue disorders					Rash, pruritus, urticaria	
General disorders and administration site conditions					Fatigue, weakness	

* A very small number of spontaneous reports have been identified following prolonged treatment with intranasal fluticasone propionate.

** Nasal septal perforation has been reported following the use of intranasal corticosteroids.

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

Growth retardation has been reported in children receiving nasal corticosteroids. Growth retardation may be possible in adolescents, too.

In rare cases osteoporosis was observed if nasal glucocorticoids were administered long-term.

OVERDOSE AND TREATMENT

With the nasal route of administration overdose reactions are not anticipated.

There are no data from patients available on the effects of acute or chronic overdosage with intranasal fluticasone propionate.

Intranasal administration of 2 milligrams fluticasone propionate (10 times the recommended daily dose) twice daily for seven days to healthy human volunteers has no effect on hypothalamo-pituitary-adrenal (HPA) axis function.

Administration of doses higher than those recommended over a long period of time may lead to temporary suppression of adrenal function. In these patients, treatment with Azelastine hydrochloride + Fluticasone propionate (Dymista) Nasal Spray should be continued at a dose sufficient to control symptoms; the adrenal function will recover in a few days and can be verified by measuring plasma cortisol.

In the event of overdose after incidental oral uptake, disturbances of the central nervous system (including drowsiness, confusion, coma, tachycardia and hypotension) caused by azelastine hydrochloride are to be expected based on the results of animal experiments.

Treatment of these disorders must be symptomatic. Depending on the amount swallowed, gastric lavage is recommended. There is no known antidote.

STORAGE CONDITIONS

Do not refrigerate or freeze.

Store at temperatures not exceeding 30°C.

Shelf-life: Bottle with 23 g suspension in 25 ml bottles: 24 months

In-use shelf life (after first use): 3 months

DOSAGE FORM AND PACKAGING AVAILABLE

Type I amber glass bottle fitted with a spray pump, a nasal polypropylene applicator (actuator) and a dust cap, 23 g (at least 120 actuations) suspension.

Pack sizes:

1 bottle with 23 g suspension in 25 ml bottles (at least 120 actuations)

NAME AND ADDRESS OF MARKETING AUTHORISATION HOLDER

Viatris Pharmaceuticals, Inc., 22nd floor, Units C&D, Menarco Tower 32nd St. Bonifacio Global City, Taguig City, Metro Manila

NAME AND ADDRESS OF MANUFACTURER

Cipla Limited, Plot No. 9 & 10, Indore Special Economic Zone, Phase II, Pithampur, District Dhar, Madhya Pradesh, IN-454 775, India

CAUTION

Foods, Drugs, Devices, and Cosmetics Act Prohibits dispensing without prescription

ADR REPORTING

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

REGISTRATION NUMBER

DR-XY47527

DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 November 2021

DATE OF REVISION OF PACKAGE INSERT

12 September 2023 Version 1.1

VIATRIS

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VIATRIS

Description	Dymista Nasalspray Suspension 137mcg/50mcg 23g			**Date: 28/Sep/22**		**Time: 10:45**	
Component Type	Leaflet	**Pharma Code**	21095454	**No. of colours**	1	**Page Count**	2/2
Affiliate Item Code	2799958	**Viatris SAP No.**	400561079	**Colours**	Black		
Superseded Affiliate Item Code	2744703	**Vendor Job No.**	Studio Oberländer	**Non-Print Colours**			
TrackWise/GLAMS Job No.	2799958	**Artwork Proof No.**	5	**Equate CMYK with**			
MA No.	DR-XY47527	**Client Market**	Philippines				
Packing Site/Printer	Cipla Ltd Unit III (Pithampur - IN)	**Keyline/Drawing No.**	Dymista_Nasalspray PIL 900 x 200 (75 x 30mm) [Physician+Patient].pdf	**Main Font**	Avant Garde Gothic	**Body Text Size**	9 pt
New Supplier Code	21095454	**Barcode Info**	n/a				
Superseded Supplier Code	2744703	**3D Render ID**	n/a	**Dimensions**	900 x 200 mm	**Min Text Size used**	7 pt
Sign-offs							
							V1 Mar 2022

21095454