



Dear Doctor,

**IMPORTANT SAFETY INFORMATION RE REMOVAL OF PRIMARY NOCTURNAL ENURESIS INDICATION FROM DESMOPRESSIN NASAL FORMULATIONS**

**DDAVP Desmopressin nasal drops solution PA1009/001/001**  
**Desmospray Desmopressin Nasal Spray PA1009/005/001**

Following review by European regulatory authorities, including the IMB, the indication for the treatment of primary nocturnal enuresis (PNE) has been removed from all desmopressin nasal spray products, including DDAVP Desmopressin nasal drops solution and Desmospray, Desmopressin Nasal Spray which are marketed by Ferring (Ireland) Limited. The other authorised indications remain as before. In comparison with oral formulations of desmopressin, nasal forms were associated with the majority of serious adverse drug reactions (ADRs) reported in patients with PNE. Rare, serious ADRs included hyponatraemia, water intoxication and convulsions.

As the risk benefit profile of the oral formulations is more favourable than the nasal spray, **the nasal form should no longer be used for the treatment of PNE in adults and children.**

Prescribers should also be aware that there is a possible risk of severe hyponatraemia when a nasal desmopressin formulation is used to treat patients with cranial diabetes insipidus.

**Further Information**

Desmopressin is a synthetic analogue of vasopressin with increased antidiuretic activity and a prolonged duration of action in comparison with the natural peptide. The nasal spray has greater bioavailability than the oral formulation. Both forms produce a sustained decrease in urine output and a decrease in plasma osmolality which can result in hyponatraemia and water intoxication particularly in the presence of inappropriate fluid intake. Hyponatraemia is a rare but serious ADR, which has been reported at a rate of approximately 15 cases per 100,000 patient years of exposure for nasal formulations and 5 cases per 100,000 patient years for oral formulations, and has been predominantly associated with overdose, excessive fluid intake or

inappropriate use. It is not known whether these adverse effects are dose-related but there is strong evidence of a relationship to the formulation. Since the majority of cases of hyponatraemia occurred with the nasal formulation in the PNE indication, only oral formulations should be used in the management of PNE. The risk of hyponatraemia occurring with oral desmopressin can be further reduced by closely following the advice in the Summary of Product Characteristics (SPC) and the Patient Information Leaflet (PIL).

### **Changes to the Summary of Product Characteristics (SPC)**

#### *Section 4.1 Therapeutic Indications*

Remove: 'The treatment of primary nocturnal enuresis'

#### *Section 4.4 Special Warnings and Precautions for Use*

Add: 'There is some evidence from post-marketing data for the occurrence of severe hyponatraemia in association with the nasal spray formulation of desmopressin, when it is used in the treatment of cranial diabetes insipidus.'

There are also further consequential changes to the remainder of the SPCs, copies of which are attached.

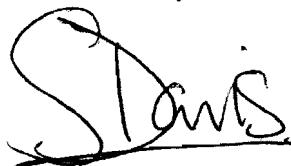
### **Reporting of suspected adverse events**

Please report any cases of suspected adverse reactions in association with the use of desmopressin to Ferring (Ireland) Limited or the IMB in the usual way. Adverse reaction report forms can be downloaded from the publications section of the IMB website at [www.imb.ie](http://www.imb.ie).

### **Communication information**

If you have any enquiries or need additional information, please contact 00353 (0)1 463 7355 Medical Information Department at Ferring Ireland Ltd, United Drug House, Magna Drive, Magna Business Park, Citywest Road, Dublin 24. The following number is available for out of hours medical emergencies: 086 6006046

Yours Sincerely,

A handwritten signature in black ink that reads "Sean Davis". The signature is written in a cursive style with a large, stylized 'S' at the beginning.

Sean Davis  
General Manager

## Summary of Product Characteristics

### 1. TRADE NAME OF THE MEDICINAL PRODUCT

DDAVP Desmopressin 100 micrograms/ml Nasal drops, solution.

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of the nasal solution contains desmopressin acetate 100 micrograms.

For excipients, see 6.1

### 3. PHARMACEUTICAL FORM

Nasal drops, solution.

Clear, colourless aqueous solution.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

1) For the diagnosis and treatment of cranial diabetes insipidus including post-hypophysectomy polyuria/polydipsia.

2) For the measurement of the urine concentration capacity.

#### 4.2 Posology and method of administration

##### **Treatment of Diabetes Insipidus:**

##### Adults :

10 to 20 micrograms once or twice daily (equivalent to 0.1ml to 0.2ml once or twice daily).

##### Children :

5 to 10 micrograms once or twice daily (equivalent to 0.05ml to 0.1ml once or twice daily). A lower dose may be required for infants.

Fluid restriction should be observed, please see section 4.4 Special Warnings and Precautions for Use.

##### **Diagnosis of Diabetes Insipidus:**

##### Adults and children :

A single dose of 20 micrograms (0.2ml)

Fluid restriction should be observed, please see section 4.4 *Special Warnings and Precautions for Use*.

##### **Renal Function Testing:**

To establish renal concentration capacity, the following single doses are recommended:

Adults :

A single dose of 40 micrograms (0.4ml).

Children ( 1-15 years ) :

A single dose of 20 micrograms (0.2ml).

Infants :

A single dose of 10 micrograms (0.1ml).

After administration of Desmopressin Intranasal Solution, any urine collected within one hour is discarded. During the next 8 hours two portions of urine are collected for osmolality testing. Fluid restriction should be observed, please see section *4.4 Special Warnings and Precautions for Use*.

### **4.3 Contra-indications**

DDAVP/Desmopressin Intranasal Solution is contraindicated in cases of :

- habitual or psychogenic polydipsia (resulting in a urine production exceeding 40 ml/kg/24 hours). Before prescribing Desmopressin Intranasal Solution the diagnoses of psychogenic polydipsia and alcohol abuse should be excluded
- history of known or suspected cardiac insufficiency and other conditions requiring treatment with diuretic agents
- known Hyponatraemia
- syndrome of inappropriate ADH secretion (SIADH)
- moderate and severe renal insufficiency ( creatinine clearance below 50ml/min).
- hypersensitivity to Desmopressin, or any of the excipients.

### **4.4 Special warnings and special precautions for use**

DDAVP Desmopressin Intranasal Solution should only be used in patients where orally administered formulations are not feasible.

Use of the product should be under specialist supervision with appropriate facilities available for monitoring and interpretation of responses

DDAVP/Desmopressin Intranasal Solution should be used with caution in :

- Very young and elderly patients,
- Conditions characterised by fluid and/or electrolyte imbalance,
- Patients at risk for increased intracranial pressure

The product should be used with caution in patients with hypertension.

Adjustment of dosage in cases immediately post-hypophysectomy should be controlled on the basis of measurements of urinary osmolality.

Special Warnings

When DDAVP/Desmopressin Intranasal Solution is prescribed it is recommended

- To start at the lowest dose
- To ensure compliance with fluid restrictions instructions
- To increase dose progressively, with caution
- To ensure that in children, administration is under adult supervision in order to control the dose intake.

Care should be taken with patients who have reduced renal function and/or cardiovascular disease or cystic fibrosis.

Patients should be warned to avoid ingesting water while swimming and to discontinue DDAVP Nasal drops during an episode of vomiting and/or diarrhoea until their fluid balance is once again normal.

There is some evidence from post-marketing data for the occurrence of severe hyponatraemia in association with the nasal spray formulation of desmopressin, when it is used in the treatment of cranial diabetes insipidus.

Renal concentration capacity test in children below the age of 1 year should only be performed under carefully supervised conditions in hospital. When used for diagnostic purposes the fluid intake must be limited to a maximum of 0.5L to quench thirst from 1 hour before until 8 hours after administration.

#### Precautions

Severe bladder dysfunction and outlet obstruction should be considered before starting treatment with desmopressin.

Precautions to avoid hyponatraemia, including careful attention to fluid restriction and more frequent monitoring of serum sodium, must be taken in case of concomitant treatment with drugs, which are suspected to induce SIADH e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine and in case of concomitant treatment with NSAID.

Treatment with desmopressin should be carefully adjusted during acute intercurrent illness characterized by fluid and/or electrolyte imbalance ( such as systemic infections, fever, gastroenteritis).

#### 4.5 Interactions with other medicaments and other forms of interaction

Indomethacin may augment the magnitude but not the duration of response to Desmopressin.

Substances, which are suspected to induce SIADH, e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect leading to an increased risk of fluid retention/hyponatraemia (see section 4.4 *Special Warnings and Precautions for Use*).

NSAIDs may induce fluid retention/hyponatraemia (see section 4.4 *Special Warnings and Precautions for Use*).

#### 4.6 Pregnancy and lactation

##### **Pregnancy**

Published data on a limited number (n = 53) of exposed pregnancies in women with diabetes insipidus indicate no adverse effects of desmopressin on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

#### **Lactation**

Results from analyses of milk from nursing mothers receiving high dose Desmopressin (300 micrograms intranasally) indicate that the amounts of Desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

#### **4.7 Effects on ability to drive and use machines**

None

#### **4.8 Undesirable effects**

Treatment without concomitant reduction of fluid intake may lead to fluid retention /hyponatraemia with or without accompanying warning signs and symptoms (headache, nausea/ vomiting, decreased serum sodium, weight gain and in severe cases convulsions).

Common (> 1/100)

General: Headache

Gastro Intestinal: Abdominal pain, nausea.

Upper respiratory: Nasal congestion/ rhinitis, epistaxis

Very rare (< 1/10000)

Metabolism : Hyponatraemia

Post marketing experience:

Isolated cases of emotional disturbances in children have been reported.

Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.

#### **4.9 Overdose**

Overdose of DDAVP/Desmopressin Intranasal Solution can cause prolonged antidiuretic effect, which may lead to fluid retention and hyponatraemia if fluid intake is not limited.

Treatment:

Although the treatment of hyponatraemia should be individualized, the following general recommendations can be given: Interruption of the desmopressin treatment, restrict fluid intake and symptomatic treatment as necessary.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Desmopressin is a structural analogue of vasopressin, with two chemical changes namely desamination of the N-terminal and replacement of the 8-L-Arginine by 8-D-Arginine. These changes have increased the antidiuretic activity and prolonged the duration of action. The pressor activity is reduced to less than 0.01% of the natural peptide as a result of which side-effects are rarely seen.

## **5.2 Pharmacokinetic properties**

Following intranasal administration, the bioavailability of Desmopressin is of the order of 10%.

Pharmacokinetic parameters following intravenous administration were reported as follows:

Total clearance : 2.6ml/min/kg body weight.

T  $\frac{1}{2}$ : 55 mins

Plasma kinetics of DDAVP in man

H .Vilhardt, S. Lundin, J. Falch.

Acta Pharmacol. ET. Toxicol. 1986, 58, 379-381

## **5.3 Preclinical safety data**

There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections of the SPC.

# **6. PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Sodium Chloride  
Chlorobutanol  
Hydrochloric Acid (for pH adjustment)  
Purified Water

## **6.2 Incompatibilities**

Not applicable

## **6.3 Shelf-life**

3 years.

## **6.4 Special precautions for storage**

Stored in a refrigerator at 2°C to 8°C.  
Do not freeze.  
Keep the container in the outer carton.

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

Amber, Type I Ph.Eur. glass vial fitted with a dropper closure and containing 2.5ml (nominal volume) of a clear aqueous solution. accompanied with a calibrated plastic tube (rhynyle) for administration.

## **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

**Instructions for use of DDAVP/Desmopressin Nasal drops, solution:**

1. Pull plastic tag on neck of bottle.
2. Break security seal and remove plastic cap.
3. Twist off the small knurled seal from the dropper. Use the same seal reversed to prevent subsequent leakage, especially if the bottle is not stored upright.
4. Take the calibrated part of the plastic tube (rhinyle) in one hand and place the fingers of the other hand around the cylindrical part of the dropper. Insert the top of the dropper in a downward position into the end of the rhinyle marked with an arrow and squeeze the dropper until the solution has reached the desired mark. The unnumbered mark between the end and the 0.05ml mark is approximately at the 0.025ml position. If difficulty is experienced in filling the rhinyle, a diabetic or tuberculin syringe may be used to draw up the dose and load the rhinyle.
5. Hold the rhinyle with the fingers approximately  $\frac{3}{4}$  inch from the end and insert it into the nostril until the tips of the fingers reach the nostril.
6. Put the other end of the rhinyle into the mouth. Hold the breath, tilt back the head and then blow with a short strong puff through the rhinyle so that the solution reaches the right place in the nasal cavity. Through this procedure, medication is limited to the nasal cavity and the preparation does not pass down into the back of the throat.
7. If this product is for a child, the dose should be given or supervised by an adult.
8. After use, close the bottle with the plastic cap, wash the rhinyle in water and shake thoroughly, until no more water is left. The rhinyle can then be used for the next application.

**7.     MARKETING AUTHORISATION HOLDER**

Ferring Ireland Ltd  
United Drug House  
Magna Drive  
Magna Business Park  
Citywest Road  
Dublin 24

**8.     MARKETING AUTHORISATION NUMBER**

PA 1009/1/1

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

25th March 1976 / 25th March 2006

**10.    DATE OF (PARTIAL) REVISION OF THE TEXT**

April 2007



## Summary of Product Characteristics

### 1. TRADE NAME OF THE MEDICINAL PRODUCT

Desmospray, Desmopressin Nasal Spray

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Desmospray contains 10 micrograms of desmopressin acetate per actuation (0.1ml)

### 3. PHARMACEUTICAL FORM

Nasal spray, solution.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Desmospray is indicated for:

i)	The treatment of nocturia associated with multiple sclerosis.
ii)	The diagnosis and treatment of vasopressin-sensitive cranial diabetes insipidus.
iii)	Establishing renal concentration capacity.

#### 4.2 Posology and Method of Administration

##### *Treatment of Nocturia associated with multiple sclerosis*

For multiple sclerosis patients up to 65 years of age with normal renal function suffering from nocturia the dose is one or two sprays intranasally (10 to 20 micrograms) at bedtime. Not more than one dose should be used in any 24 hour period. If a dose of two sprays is required, this should be as one spray into each nostril.

Fluid restriction should be observed, please see section 4.4 *Special Warnings and Precautions for Use*. In the event of signs of fluid retention/hyponatraemia, treatment should be interrupted.

##### *Treatment of Diabetes Insipidus:*

Dosage is individual but clinical experience has shown that the average maintenance dose in adults is one or two sprays (10 to 20 micrograms) once or twice daily. If a dose of two sprays is required, this should be as one spray into each nostril. For children, the dose is one spray (10 micrograms), once or twice daily.

##### *Diagnosis of Diabetes Insipidus:*

The diagnostic dose in adults and children is two sprays (20 micrograms). Failure to elaborate concentrated urine after water deprivation, followed by the ability to do so after the administration of Desmospray confirms the diagnosis of cranial diabetes insipidus. Failure to concentrate after the administration suggests nephrogenic diabetes insipidus.

Fluid restriction should be observed, please see section 4.4 *Special Warnings and Precautions for Use*.

### ***Renal Function Testing***

**To establish renal concentration capacity, the following single doses are recommended**

Adults: Two sprays into each nostril (a total of 40 micrograms).

Children: (1- 15 years): One spray into each nostril (a total of 20 micrograms).

Infants (to 1 year): One spray (10 micrograms).

Adults and children with normal renal function can be expected to achieve concentrations above 700mOsm/kg in the period of 5-9 hours following administration of Desmospray. It is recommended that the bladder should be emptied at the time of administration. After administration of Desmospray, any urine collected within one hour is discarded. During the next 8 hours two portions of urine are collected for osmolality testing. Fluid restriction should be observed, please see section 4.4 *Special Warnings and Precautions for Use*.

In normal infants a urine concentration of 600mOsm/kg should be achieved in the 5 hour period following the administration of Desmospray. The fluid intake at the two meals following the administration should be restricted to 50% of the ordinary intake in order to avoid water overload.

### **4.3 Contraindications**

Desmospray is contraindicated in cases of:

- habitual or psychogenic polydipsia (resulting in a urine production exceeding 40 ml/kg/24 hours). Before prescribing Desmospray the diagnoses of psychogenic polydipsia and alcohol abuse should be excluded.
- history of known or suspected cardiac insufficiency and other conditions requiring treatment with diuretic agents
- known Hyponatraemia
- syndrome of inappropriate ADH secretion (SIADH)
- moderate and severe renal insufficiency (creatinine clearance below 50ml/min).
- hypersensitivity to Desmopressin, the preservative benzalkonium chloride or any of the excipients.

When used to control nocturia in patients with multiple sclerosis, Desmopressin should not be used in patients with hypertension or cardiovascular disease.

Desmopressin should not be prescribed to patients over the age of 65 for the treatment of nocturia associated with multiple sclerosis.

### **4.4 Special warnings and precautions for use**

Use of the product should be under specialist supervision with appropriate facilities available for monitoring and interpretation of responses.

Desmospray should be used with caution in:

- Very young and elderly patients,
- Conditions characterised by fluid and/or electrolyte imbalance,
- Patients at risk for increased intracranial pressure

### **Special Warnings**

Desmospray should only be used in patients where orally administered formulations are not feasible.

When Desmospray is prescribed it is recommended

- To start at the lowest dose
- To ensure compliance with fluid restrictions instructions
- To increase dose progressively, with caution
- To ensure that in children, administration is under adult supervision in order to control the dose intake.

Care should be taken with patients who have reduced renal function and/or cardiovascular disease or cystic fibrosis.

Patients should be warned to avoid ingesting water while swimming and to discontinue Desmospray during an episode of vomiting and/or diarrhoea until their fluid balance is once again normal.

There is some evidence from post-marketing data for the occurrence of severe hyponatraemia in association with the nasal spray formulation of desmopressin, when it is used in the treatment of cranial diabetes insipidus.

When Desmospray is used in the treatment of nocturia, periodic assessments should be made of blood pressure and weight to monitor the possibility of fluid overload.

Precautions to prevent fluid overload must be taken in patients at risk for increased intracranial pressure.

Renal concentration capacity testing in children below the age of 1 year should only be performed in hospital and under careful supervision. When used for diagnostic purposes the fluid intake must be limited to a maximum of 0.5 L to quench thirst from 1 hour before until 8 hours after administration.

Due to the presence of benzalkonium chloride this product may cause bronchospasm.

#### Precautions

Severe bladder dysfunction and outlet obstruction should be considered before starting treatment with Desmopressin.

Precautions to avoid hyponatraemia, including careful attention to fluid restriction and more frequent monitoring of serum sodium, must be taken in case of concomitant treatment with drugs, which are suspected to induce SIADH e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine and in case of concomitant treatment with NSAID.

Treatment with desmopressin should be carefully adjusted during acute intercurrent illness characterized by fluid and/or electrolyte imbalance (such as systemic infections, fever, and gastroenteritis).

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

Indomethacin may augment the magnitude but not the duration of response to Desmopressin.

Substances, which are suspected to induce SIADH, e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect leading to an increased risk of fluid retention/hyponatraemia (see section 4.4 *Special Warnings and Precautions for Use*).

NSAIDs may induce fluid retention/hyponatraemia (see section 4.4 *Special Warnings and Precautions for Use*).

#### **4.6 Pregnancy and Lactation**

##### Pregnancy:

Published data on a limited number (n = 53) of exposed pregnancies in women with diabetes insipidus indicate no adverse effects of desmopressin on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Caution should be exercised when prescribing to pregnant women.

#### Lactation:

Results from analyses of milk from nursing mothers receiving high dose Desmopressin (300 micrograms intranasally) indicate that the amounts of Desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

### **4.7 Effects on Ability to Drive and Use Machines**

None

### **4.8 Undesirable Effects**

Treatment without concomitant reduction of fluid intake may lead to fluid retention /hyponatraemia with or without accompanying warning signs and symptoms (headache, nausea/ vomiting, decreased serum sodium, weight gain and in severe cases convulsions).

Common (> 1/100)

General: Headache

Gastro Intestinal: Abdominal pain, nausea.

Upper respiratory: Nasal congestion/ rhinitis, epistaxis

Very rare (< 1/10000)

Metabolism: Hyponatraemia

Post marketing experience:

Isolated cases of emotional disturbances in children have been reported.

Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.

### **4.9 Overdose**

Overdose of Desmospray can cause prolonged antidiuretic effect, which may lead to fluid retention and hyponatraemia if fluid intake is not limited.

Treatment:

Although the treatment of hyponatraemia should be individualized, the following general recommendations can be given: Interruption of the desmopressin treatment, restrict fluid intake and symptomatic treatment as necessary.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic Properties**

Desmopressin is a structural analogue of vasopressin, with two chemical changes, namely desamination of the N-terminal and replacement of the 8- L -Arginine by 8- D -Arginine. These changes have increased the antidiuretic activity and prolonged the duration of action. The pressor activity is reduced to less than 0.01% of the natural peptide as a result of which side-effects are rarely seen.

## 5.2 Pharmacokinetic Properties

Following intranasal administration, the bioavailability of Desmopressin is of the order of 10%.

Pharmacokinetic parameters following intravenous administration have been reported as follows:

Total clearance:	2.6 ml / min / kg body wt.
T $\frac{1}{2}$	55mins

Plasma kinetics of DDAVP in man

H. Vilhardt, S. Lundin, J. Falch

Acta Pharmacol et Toxicol, 1986, 58, 379-381

## 5.3 Preclinical Safety Data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of Excipients

Sodium Chloride

Citric Acid Monohydrate

Disodium Phosphate Dihydrate

Benzalkonium Chloride Solution

Purified Water

### 6.2 Incompatibilities

None known.

### 6.3 Shelf Life

2 years

### 6.4 Special Precautions for Storage

Do not store above 25°C. Store in original carton.

### 6.5 Nature and contents of container

The spray pack comprises of a 10ml amber glass injection vial fitted with a snap- on tamper-proof pre- compression pump spray, to which a 20mm nasal adaptor is attached. The fill volume is 7.1ml including overage to allow delivery of 60 doses of 0.1 ml.

### 6.6 Instructions for use and handling

Before Desmospray is used for the first time, prime the pump by pressing downward 4 times or until an even spray is obtained. If the spray has not been used for a week it will be necessary to prime the pump again by pressing it downwards once or twice until an even spray is obtained.

Instructions for use:

The patient should blow his/her nose before using the spray.

1. Remove the protection cap.
2. Control that the end of the tube inside the bottle is submerged in the liquid.
3. Re-prime the pump if the spray has not been used within the last week.
4. Once it has been primed, the pump delivers one dose each time pressure is applied.
5. The head must be tipped back slightly while inserting the applicator straight into the nostril.
6. When a higher dose is needed, spray alternatively into each nostril.
7. Replace cap after use and store the bottle in an upright position.

The spray bottle should always be stored in an upright position.

If there is any doubt concerning the correct intake of the dose, the spray should not be re-administered until the next scheduled dose.

In young children, administration should be under strict adult supervision to ensure the correct dosage.

## **7. MARKETING AUTHORISATION HOLDER**

Ferring Ireland Limited,  
United Drug House,  
Magna Drive,  
Magna Business Park,  
Citywest Road,  
Dublin 24,  
Ireland.

## **8. MARKETING AUTHORISATION NUMBER**

1009/5/1

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

9<sup>th</sup> July 1987 / 9<sup>th</sup> July 2002 / April 2007

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

April 2007.