# Part II

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Dexa-Rhinaspray Duo 120 micrograms/20 micrograms, Nasal Spray, Suspension.

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tramazoline hydrochloride 120 micrograms/metered dose and dexamethasone isonicotinate 20 micrograms/metered dose.

Also contains 150 micrograms/ml benzalkonium chloride.

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Nasal spray, suspension.

A white, homogenous suspension.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Treatment of allergic rhinitis.

### 4.2 Posology and method of administration

**Adults (including the elderly)**

1 metered dose into each nostril up to six times in 24 hours, although 2 or 3 applications a day are usually sufficient.

**Children**

5-12 years: 1 metered dose into each nostril up to twice daily.
Under 5 years: Not recommended.

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

Each course of treatment should not exceed 14 days.

No specific information on the use of this product in the elderly is available. No adverse reactions specific to this age group have been reported with tramazoline and dexamethasone.

**Administration**

For detailed information on instructions for use please refer to the Patient Information Leaflet.

Shake well each time before use.

Avoid spraying Dexa-Rhinaspray Duo in or around the eye. Should this occur, immediately flush your eye with cold tap water for several minutes.

If the nasal tip becomes clogged, remove the clear plastic dust cap. Hold the nasal tip under running warm tap water for about a minute. Dry the nasal tip, re-prime the nasal pump spray and replace the plastic dust cap.

## 4.3 Contraindications

Dexa-Rhinaspray Duo should not be used in patients with:

- Untreated infections in the nose, mouth, eye, and upper respiratory tract (e.g. herpes, vaccinia, varicella, (chickenpox), nasal mycosis, etc
- Pulmonary tuberculosis
- Rhinitis sicca
- Glaucoma (including narrow-angle glaucoma)
- Known hypersensitivity to tramazoline hydrocholoride or benzalkonium chloride or any other component of the product.

Dexa-Rhinaspray Duo should not be used after cranial surgery via the nose.

Dexa Rhinaspray Duo is not suitable for children under 5 years of age.

The use of Dexa-Rhinaspray Duo is contraindicated during pregnancy and lactation**.**

## 4.4 Special warnings and precautions for use

Care should be used to avoid contact with the eyes as conjunctival irritation may occur. The use of Dexa-Rhinaspray Duo for prolonged periods is not recommended.

The possibility of side-effects from the systemic absorption of dexamethasone should be borne in mind.

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses.

It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.

Treatment with higher than recommended doses of nasal corticosteroids may result in clinically significant adrenal suppression. If there is evidence of higher than recommended doses being used then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

Dexa-Rhinaspray Duo should be used with caution and under medical advice in patients with prostate hypertrophy and congenital pophyria.

Possibility of adrenal insufficiency when changing from systemic to local steroids, also allergies may worsen.

Higher risk of infection (e.g. TB, certain viral infections (e.g. zoster, herpes simplex, vaccinia)), opportunistic infections.

Caution in patients with diabetes mellitus or osteoporosis due to corticosteroid.

Use of vasoconstrictors requires special attention when used in patients with cardiac diseases.

Prolonged use of vasoconstrictors is not recommended and may lead to chronic inflammation (and thus to a blocked nose) and atrophy of the nasal mucous membrane.

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

In certain anti-depressant (MAO inhibitors or tricyclic anti-depressants) or vasopressor drugs are given simultaneously, effects on the cardiovascular system can lead to an increase in blood pressure. Combined use with tricyclic anti-depressants can also lead to tachyarrhythmia.

Used in combination with beta2sympathomimetic may result in an increased beta2 agonist response.

CYP3A4 inhibitors: serum level and/or toxicity of steroid component may be increased (e.g. ketoconazole, itaconazole, clotrimazole, ritonavir, ciclosporin, ethinylestradiol, troleandromycin, clarithomycin, cimetidine, diltiazem, idinavir).

CYP3A4 inducers: serum level and/ or toxicity of steroid component may be decreased (e.g. carbamazepine, phenytoin, Phenobarbital, rifampin).

Caution when combined with anti-hypertensive drugs.

## 4.6 Pregnancy and lactation

Use of Dexa-Rhinaspray Duo during pregnancy and lactation is contraindicated due to possible systemic absorption.

## 4.7 Effects on ability to drive and use machines

None stated.

## 4.8 Undesirable effects

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

The following side effects have been listed based on the possible class effects of the two components tramazoline and dexamethasone. Frequencies are not known as they cannot be estimated from the available data.

*Immune system disorders*
Hypersensitivity reactions
Masking of local signs of infection in ear, nose and throat.
Endocrine disorders
Hypercortisolims.

*Psychiatric disorders*
Hallucinations

*Nervous system disorders*
Headache
Dizziness
Insomnia
Somnolence
Sedation
Restlessness
Disturbance in sense of taste
Tiredness

*Eye disorders*
Increased Intraocular pressure

*Cardiac disorders*
Palpitations
Tachycardia
Cardiac arrhythmias
Blood pressure increase
Respiratory, Thoracic and Mediastinal Disorders
Burning of nasal mucosa
Dryness of nasal mucosa
Throat irritation
Sneezing
Nasal septal ulceration
Nasal septal perforation
Epistaxis
Mucosal swelling (rebound congestion).
Gastro-intestinal Disorders
Nausea

*Skin and subcutaneous Disorders*
Rash
Pruritus
Sweating
Urticaria

## 4.9 Overdose

In analogy with other alpha-sympathomimetics the clinical picture of an intoxication with Dexa-Rhinaspray Duo may be confusing, because phases of stimulation and depression of the CNS and cardiovascular system may alternate.

Especially in children intoxications result in CNS effects with seizures and coma, bradycardia, respiratory depression as well as an increase in blood pressure. Symptoms of stimulation of the CNS are anxiety, agitation, hallucinations and seizures. Symptoms of depression of the CNS are decrease of body temperature, lethargy, somnolence and coma.

In addition the following symptoms may occur: sweating, apprehension, nausea, mydriasis, miosis, swelling, fever, pallor, cyanosis of the lips, cardiovascular dysfunction (tachycardia, cardiac arrhythmias, bradycardia, cardiac arrest, hypertonia, shock like drop in blood pressure) respiratory dysfunction (respiratory failure, respiratory arrest) psychological alterations.

**Dexamethasone**

Chronic abuse and overdose supression of adrenal/HP axis, hypercortisolism, growth retardation in children.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Tramazoline hydrochloride is a sympathomimetic with local vasoconstrictor activity. It has a quick-acting, long lasting decongestant effect on the nasal mucosa.

Dexamethasone isonicotinate is a corticosteroid with marked anti-inflammatory and anti-allergic properties.

## 5.2 Pharmacokinetic properties

Pharmacokinetic studies with tramozoline in humans have not been carried out. The Pharmacokinetics of tramazoline has been investigated in the rat, rabbit and primates. It has been demonstrated that 50-80% of the dose is absorbed after oral or intranasal administration.

Tramazoline and its metabolites are distributed in all the internal organs, with the highest concentration being invariably found in the liver. Elimination, with a terminal half-life of 5-7 hours, is primarily renal.

So far no pharmacokinetic data are available after nasal application of dexamethasone isonicontinate. After inhalation approximately 18 mg of dexamethasone isonicotinate, maximum plasma levels of around 20 nanograms/ml are obtained. By extrapolation, a plasma level of around 0.02 nanograms/ml from a nasal spray containing 0.02 mg can be expected.

For a comparable corticosteroid beclomethasone dipropionate it has been reported that total systemic bioavailability after nasal application was even lower compared with inhalation (44 vs. 62%). This was mainly due to absorption of the orally swallowed fraction and not by absorption via the nasal mucosa.

Pharmacokinetic data on the use of dexamethasone-21-isonicotinate in laboratory animals are not available. In humans, dexamethasone-21-isonicotinate is slowly absorbed by the lungs and afterwards slowly eliminated.

Dexamethasone is readily absorbed from the gastrointestinal tract. Its biological half-life in plasma is about 190 minutes. Binding of dexamethasone to plasma proteins is about 77% which is less than for most other corticosteroids. Up to 65% of a dose is excreted in urine within 24 hours. Clearance in premature neonates is reported to be proportional to gestational age, with a reduced elimination rate in the most premature. It readily crosses the placenta with minimal inactivation.

## 5.3 Preclinical safety data

None stated.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Benzalkonium chloride
Sodium chloride
Polyoxyethylene-sorbitan monooleate (Polysorbate 80)
Glycerol 85%
Purified water
Sodium hydroxide

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf Life

2 years.

After opening use within 6 months after which discard any remaining product.

## 6.4 Special precautions for storage

Do not store above 25$^{o}$C.

## 6.5 Nature and contents of container

Amber coloured glass (Type I) bottle fitted with 0.07 ml metering pump and white nasal adaptor and a protective cap. Nominal contents 10 ml equivalent to not less than 110 doses.

## 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

No special requirements.

## 7 MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Limited
Ellesfield Avenue
Bracknell
Berkshire
RG12 8YS
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER

PA 0007/053/001

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

Date of first authorisation: 4$^{th}$ March 1999

Date of last renewal: 19$^{th}$ January 2007

## 10 DATE OF REVISION OF THE TEXT

February 2007