CONTRAINDICATIONS (RHINOCORT Powder Spray is contraindicated in the following patients.)
(1) Patients with infectious disease or systemic mycosis for which effective antimicrobial drugs are not available. [Symptoms may be exacerbated.]

(2) Patients with a history of hypersensitivity to any of the ingredients of RHINOCORT Powder Spray.

RELATIVE CONTRAINDICATIONS (As a general rule, RHINOCORT Powder Spray is contraindicated in the following patients. If the use of this Product is considered essential, it should be administered with care.)

Patients with tuberculous disease [Symptoms may be exacerbated.]

DESCRIPTION

<table>
<thead>
<tr>
<th>Brand name</th>
<th>RHINOCORT Powder Spray 25µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>Nasal dry powder</td>
</tr>
<tr>
<td>Fill weight of the container (Labeled number of spray)</td>
<td>0.9087g (60 puffs)</td>
</tr>
<tr>
<td>Active ingredient</td>
<td>Beclometasone Dipropionate</td>
</tr>
<tr>
<td>Content</td>
<td>1 container</td>
</tr>
<tr>
<td></td>
<td>1.50mg</td>
</tr>
<tr>
<td></td>
<td>1 puff</td>
</tr>
<tr>
<td></td>
<td>25µg</td>
</tr>
<tr>
<td>Inactive ingredient</td>
<td>Hydroxypropylcellulose,</td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate,</td>
</tr>
<tr>
<td></td>
<td>Stearic acid</td>
</tr>
<tr>
<td>Color / description</td>
<td>RHINOCORT Powder Spray is an all-in-one multidose drug product (with a counter device). It contains white to yellowish white powder. The powder is almost odorless and tasteless.</td>
</tr>
</tbody>
</table>

INDICATIONS
Allergic rhinitis and vasomotor rhinitis

DOSAGE AND ADMINISTRATION
Usually, one puff (25 µg of beclometasone dipropionate) is sprayed into each nasal cavity twice daily, i.e. in the morning (on awakening) and in the evening (at bedtime). The dose may be adjusted according to the patient’s symptoms.

PRECAUTIONS
1. Careful Administration (RHINOCORT Powder Spray should be administered with care in the following patients.)
(1) Patients with infection [Symptoms may be exacerbated.]
(2) Patients with recurrent nosebleeds [Bleeding may be intensified.]
(3) Patients with hypertension [Blood pressure may be elevated.]
(4) Patients with diabetes mellitus [Symptoms may be exacerbated.]

2. Important Precautions
(1) As a general rule, RHINOCORT Powder Spray should not be used in status asthmaticus or in sudden exacerbations of asthma.
(2) In patients with severe hypertrophic rhinitis or nasal polyps, concomitant treatment for reducing the symptoms to some extent is recommended in order to ensure the effect of RHINOCORT Powder Spray in the nasal cavity.
(3) If nasal symptoms are exacerbated during administration of RHINOCORT Powder Spray, antihistaminic drugs or systemic steroids should be used concomitantly for a short period, and the dose of the concomitant drug should gradually be reduced as the symptoms become milder.
(4) Since RHINOCORT Powder Spray has prolonged effects, especially in a long-term administration in the patients of
perennial rhinitis, an effort should be made to reduce the dose or suspend administration of RHINOCORT Powder Spray when symptom improvement is maintained.

(5) **Dose reduction of systemic steroids should be conducted gradually** in response to the symptom stabilization after the start of inhaling RHINOCORT Powder Spray. The dose reduction should be conducted according to the usual dose-reducing procedure for steroids.

(6) Since **adrenocortical insufficiency** is suspected in patients on long-term or massive systemic steroid therapy, adrenocortical function should be monitored during dose reduction or after withdrawal of systemic steroids, and attention should be paid to such stresses as injuries, surgeries, and severe infections. If necessary, the dose of systemic steroids should be temporarily increased.

(7) **Dose reduction and withdrawal of systemic steroids** may be associated with the occurrence or exacerbation of bronchial asthma, and occasionally such symptoms as eczema, urticaria, dizziness, palpitation, malaise, hot flushes facial, and conjunctivitis. (Appropriate measures should be taken when such symptoms are noted.)

### 3. Adverse Reactions

Eleven (11) adverse drug reactions were observed in 11 (2.6%) of 420 patients evaluated for safety at the time of evaluation. The major adverse reactions were nasal symptoms, including 2 events of nasal cavity irritation (0.5%), 1 event of nasal cavity foreign body feeling (0.2%), 1 event of sensation of nasal congestion (0.2%), 1 event of dysosmia (0.2%), etc. Change in laboratory test result considered as adverse reaction was 1 event of serum cortisol increased (0.2%).

#### (1) Clinically significant adverse reactions

**Eyes:** Intraocular pressure increased and glaucoma have been reported outside Japan. Appropriate measures, such as discontinuation of use, should be taken if such symptoms are noted.

#### (2) Other adverse reactions

<table>
<thead>
<tr>
<th>Type/Incidence</th>
<th>Incidence unknown</th>
<th>5%≥0.1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>Rashles including urticaria, erythema, itching, edema, etc.</td>
<td></td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>Infection</td>
<td>Nasal cavity irritation, nasal cavity foreign body feeling, sensation of nasal congestion, dysosmia</td>
</tr>
<tr>
<td>Psychoneurologic</td>
<td>Headache/headache dull, sensation of block in ear</td>
<td></td>
</tr>
<tr>
<td>Oral and respiratory</td>
<td>Sensation of pharyn dry</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>Serum cortisol increased</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>Nasal septum perforation</td>
<td></td>
</tr>
</tbody>
</table>

Note 1) Appropriate measures, e.g. discontinuation of administration, should be taken if such adverse drug reactions are noted.

Note 2) According to the spontaneous reports and/or reports on other beclometasone dipropionate preparations.

Note 3) Frequency of inhalation should be decreased or inhalation should be discontinued.

### 4. Use in the Elderly

Since elderly often have reduced physiological functions, RHINOCORT Powder Spray should be used with caution while monitoring the patient’s condition and paying attention to the duration of administration, etc.

### 5. Use during Pregnancy, Delivery or Lactation

RHINOCORT Powder Spray should be used to pregnant or possibly pregnant women only if the expected therapeutic benefits outweigh the possible risks associated with treatment. [Teratogenicity has been reported in animal experiments.]

### 6. Pediatric Use

(1) Since RHINOCORT Powder Spray is a steroid preparation, it should be used only when remission of symptoms cannot be achieved with nonsteroidal drugs.

(2) **Use over a prolonged period or in large amounts may lead to impairment of growth.** When RHINOCORT Powder Spray is used, instructions for proper use should be given and the clinical course should be carefully monitored.

(3) **Due to the difficulty of spray device manipulation or inhalation,** there has been no experience with use in low birth weight infants, newborns, infants, or children 5 years of age or younger.

### 7. Overdosage

Overdosage may result in suppression of pituitary adrenal system function. When the suppression persists over a prolonged period, symptoms similar to those observed after systemic administration of adrenocortical steroids may appear. In such cases, the dose of RHINOCORT Powder Spray should be gradually reduced by the same procedure as for discontinuation of systemic steroids.

### 8. Precautions Concerning Use

(1) **Route of administration**

1) Use RHINOCORT Powder Spray for nasal spraying only.

2) Never inhale RHINOCORT Powder Spray into the oral cavity for the treatment of bronchial asthma.

3) Never spray RHINOCORT Powder Spray onto the eyes.

(2) **For administration**

If patients have a large amount of nasal discharge, they should be advised to blow their nose, and then spray RHINOCORT Powder Spray and inhale it.

(3) **Available number of sprays**

One container of RHINOCORT Powder Spray can deliver 60 puffs. Patients should be instructed not to exceed the limits.

### 9. Other Precautions

Nasal congestion may occur as an adverse reaction to such antihypertensive drugs as reserpin-type agents and
α-methyldopa preparations. When RHINOCORT Powder Spray is administered to patients with allergic rhinitis or vasoconstrictive rhinitis taking such antihypertensive drugs, the effect of this Product on the symptoms of nasal congestion may be masked. Therefore, RHINOCORT Powder Spray should be administered with careful clinical observation.

PHARMACOKINETICS

(Reference information)

Intranasal distribution, adhesion and retention properties
Intranasal distribution, adhesion and retention properties were investigated by using 3H-labeled beclometasone dipropionate as the active ingredient and hydroxypropylcellulose as adhesive base, and the following results were obtained.

1. When intranasally administered to anesthetized rabbits, beclometasone dipropionate was distributed mainly in the anterior nasal turbinate of the anterior part of the nasal cavity 5 minutes after administration. And it was distributed over the entire nasal cavity 120 minutes after administration.1)

2. When intranasally administered to anesthetized rabbits, residual radioactivity as a percentage of the dose administered was 76.4%, 41.0%, and 12.7% at 5, 120, and 240 minutes after administration, respectively.2)

CLINICAL STUDIES

Clinical effects
The efficacy rate in the 416 patients included in the evaluation of efficacy in the clinical studies, including comparative clinical studies, conducted at a total of 152 institutions in Japan was as follows,3),9)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Effective or better</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic rhinitis</td>
<td>83.2% (298/358)</td>
</tr>
<tr>
<td>Vasomotor rhinitis</td>
<td>62.1% (36/58)</td>
</tr>
</tbody>
</table>

PHARMACOLOGY

1. Anti-inflammatory action
In the vasoconstriction study in human skin, beclometasone dipropionate exhibited a local anti-inflammatory action approximately 5 times stronger than that of triamcinolone acetonide and approximately 600 times stronger than that of dexamethasone.10)

2. Prevention against challenge reactions
A quantitative nasal mucosal challenge test was performed using house dust antigen in adult patients with perennial nasal allergy, and changes in nasal respiratory resistance were investigated during repeated administration of 3µg/day, 25µg/day, 50µg/day and 100µg/day of beclometasone dipropionate for one week. The results revealed dose-dependent decrease of both the susceptibility and reactivity of the nasal mucosa to the antigen, showing preventive inhibition of nasal respiratory resistance induced by nasal mucosal challenge. The inhibitory effect coincided with the effect in improving the clinical nasal symptoms (sneezing, rhinorrhea, and nasal congestion).11)

PHYSICOCHEMISTRY

Nonproprietary name: Beclometasone Dipropionate

Chemical name: 9-Chloro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3, 20-dione 17, 21-dipropionate

Structural formula:

Molecular formula: C28H37ClO3
Molecular weight: 521.04
Melting point: approximately 208°C (with decomposition)

Description: Beclometasone dipropionate occurs as white to pale yellow powder. It is odorless. It is freely soluble in chloroform, soluble in methanol, sparingly soluble in ethanol (95) and in 1,4-dioxane, slightly soluble in diethyl ether, and practically insoluble in water.

PRECAUTIONS FOR HANDLING

(1) Give the attached instruction leaflet and storage bag to the patients, and adequately instruct them how to use the apparatus.

(2) Since this RHINOCORT Powder Spray is sealed in aluminum package for moisture prevention, patient should be instructed to put the drug into the attached storage bag and store away from high temperature and humidity after opening.

(3) Never use RHINOCORT Powder Spray that passed over a long period of time after opening the aluminum package.

PACKAGING

10 containers

REFERENCES


REQUESTS FOR LITERATURE SHOULD BE MADE TO:
Sales Training & Information Department
TEIJIN PHARMA LIMITED
2-1, Kasumigaseki 3-chome, Chiyoda-ku, Tokyo 100-8585
Toll-Free: 0120-189-315

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