SUMMARY OF PRODUCT INFORMATION

1. NAME OF MEDICINAL PRODUCT
BECLOSP 100 mcg nasal spray, suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active substance
Beclomethasone dipropionate.....100 micrograms/spray

Excipients
Benzalkonium chloride 50% aqueous solution.....0,45 mg/mL
See section 6.1 for excipients.

3. PHARMACEUTICAL FORM
Nasal spray
White or off-white suspension in an amber PET bottle

4. CLINICAL PROPERTIES
4.1. Therapeutic indications
It is indicated for the symptomatic treatment and prophylaxis of perennial (year-round) allergic rhinitis, seasonal allergic rhinitis and vasomotor rhinitis.

4.2. Posology and method of application
Posology/frequency and duration of administration:
Adults and children over 6 years of age:
The recommended dose is two sprays in each nostril once daily. The first spray should be in the upper part of the nasal cavity and the second spray in the lower part of the nasal cavity. Total daily administration should not normally exceed 4 sprays (400 micrograms). Regular use is essential for full therapeutic benefit. The patient's compliance with the regular dosage regimen should be ensured and the patient should be informed that nasal relief will be achieved several days after administration.

It should not be used in children under 6 years of age.

Method of administiration:
BECLOSP is only administered intranasally. When there is excessive mucus secretion and edema in the nasal mucosa, the drug may not reach the place where it will show its effect. In this respect, the nose should be thoroughly cleaned before using the nasal spray.
The bottle should be shaken well before each application. In addition, before starting treatment, it is recommended to remove the protective cap and protective ring and run the pump several times until the solution is released.
Additional information for special populations

Renal/hepatic failure:
No data available.

Pediatric population:
In children under 6 years of age, clinical data are insufficient to recommend use.

Geriatric population:
No data available.

4.3. Contraindications
BECLOSP is contraindicated in patients with a history of hypersensitivity to any of the ingredients of the drug and in local viral (herpes) and tubercular infections.

It should not be used in children under 6 years of age.

4.4. Special warnings and precautions for use
Long-term and high dose use of nasal corticosteroids may lead to systemic effects. These systemic effects may manifest as Cushing's syndrome, Cushing's-like symptoms, adrenal suppression, slowed growth in children and adolescents, decreased bone mineral density, cataracts, glaucoma and, less commonly, psychological or behavioral side effects such as disturbed sleep patterns, anxiety, depression and aggression (especially in children) or neurological side effects such as psychomotor hyperactivity. In such cases, treatment with BECLOSP should be discontinued and appropriate treatment should be started. Systemic effects have been reported with nasal corticosteroids, especially with high doses and long term use. These effects occur much less frequently than with oral corticosteroids and vary both between individuals and between corticosteroid preparation.

In the treatment of seasonal and perennial allergic rhinitis, improvement is seen after a few days; in some patients it may take up to two weeks for all symptoms to disappear. If there is no significant improvement in symptoms after three weeks of use, BECLOSP should be discontinued. It should not be used for longer than 1 month without consulting a doctor.

Unless prescribed by a physician, BECLOSP nasal spray should not be used until healing occurs, as with other corticosteroids, as it may delay the healing of new wounds caused by various reasons such as nasal surgical procedures, trauma, nasal septal ulcers.

Infections of the nasal passages and paranasal sinuses, pulmonary tuberculosis, untreated fungal, local bacterial or viral infections and ocular herpes simplex should be treated appropriately before starting treatment with BECLOSP.

Excessively prolonged use of topical corticosteroids may cause transient suppression of the hypothalamic-pituitary-adrenal (HPA) axis and thus secondary adrenal insufficiency.

Caution should be exercised when switching patients treated with systemic corticosteroids to BECLOSP if there is a condition that may cause adrenal dysfunction. Although systemic treatment administered every other day reduces the possibility of HPA suppression, caution should be exercised when switching from systemic steroid treatment to BECLOSP treatment. Patients receiving systemic corticosteroid treatment should use this product only under the supervision of their physician.

Systemic effects such as osteoporosis, peptic ulcer or secondary adrenal insufficiency symptoms may develop if the recommended doses of intranasal beclomethasone are exceeded or in those with special individual sensitivities or sensitized due to recent systemic steroid treatment.

It has been reported that growth retardation may occur with the use of nasal corticosteroids in children over six years of age. Growth rate should be kept under control during long-term treatment in children. If growth rate is slow, consideration should be given to reducing the treatment dose to the lowest dose that will provide symptom control.

There are insufficient clinical data on its use in children under six years of age.

Although BECLOSP controls seasonal allergic rhinitis in most cases, additional treatment may be required in cases of exposure to seasonal allergens, especially for the control of eye symptoms.

Visual disturbances related to systemic and topical corticosteroid use may be reported. If the patient experiences blurred vision or other visual disturbances, the patient should be referred to an ophthalmologist to evaluate possible causes, which may include cataracts, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR), which has been reported after systemic and topical corticosteroid use.
BECLOSP contains 0.03 mg benzalkonium chloride in each spray. Long-term use may cause edema of the nasal mucosa.

4.5. Interaction with other medicinal products and other forms of interaction
Beclomethasone is less dependent on CYP3A metabolism than other corticosteroids and interactions are generally unlikely. However, caution and adequate monitoring of the use of these agents is recommended, as the possibility of systemic effects cannot be ruled out with concomitant use with strong CYP3A inhibitors (e.g. ritonavir, cobicistat).

Additional information on special populations
No interaction studies have been conducted on special populations.

Pediatric population
No interaction studies have been conducted on the pediatric population.

4.6. Pregnancy and lactation
General advice
Pregnancy category: C

Women of childbearing potential/Contraception
There are insufficient data on the use of beclomethasone dipropionate in women of childbearing potential and on the effect of contraception. Animal studies have shown reproductive toxicity (see Section 5.3). The potential risk to humans is not known.

Pregnancy
There is insufficient evidence on the safety of beclomethasone dipropionate for use in pregnant women. In animal reproduction studies, potent adverse effects typical of corticosteroids were seen only at high levels of systemic exposure. Direct intranasal administration ensures minimal systemic exposure. Use of the drug during pregnancy should be considered only if the expected benefit to the mother is greater than the risk to the fetus.

Lactation
It is thought that beclomethasone dipropionate is excreted in breast milk, but significant levels in breast milk are unlikely at doses used for direct intranasal administration. When used in breastfeeding mothers, the potential harm to mother and infant should be weighed against the therapeutic benefits.

Reproductive ability/Fertility
No data available.

4.7. Effects on the ability to drive and use machines
BECLOSP does not affect the ability to drive and use machines.

4.8. Undesirable effects
Very common, common and uncommon effects were generally described based on clinical data. Rare and very rare effects were based on spontaneous data. In the frequency definition of undesirable effects, rates in the placebo groups are not considered since they are comparable to rates in the active treatment group.

The frequency classification is as follows:
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); unknown (cannot be estimated from available data)

Systemic side effects are unlikely due to the low doses used. Intranasal corticosteroids can cause systemic side effects such as growth arrest in children and adolescents, especially if prescribed in high doses for a long period of time. Therefore, extreme caution should be exercised with prolonged use of the product and the patient should be closely monitored to detect any possible systemic side effects (such as osteoporosis, peptic ulcer, signs of secondary adrenal insufficiency) immediately.

Immune system diseases
Hypersensitivity reactions;
Common: Rash, urticaria, pruritus, erythema
Very rare: Anaphylactic reactions such as angioedema, dyspnea and/or bronchospasm, edema of the eyes, face, lips and throat

Nervous system disorders
Common: Unpleasant taste and odor

Eye diseases
Very rare: Glaucoma, increased intraocular pressure, cataract
Unknown: Blurred vision (see Section 4.4)

Respiratory, chest and mediastinal disorders
Common: Epistaxis, dry nose, nasal irritation, dry throat, throat irritation
Very rare: Nasal septal perforation

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose and treatment
The only harmful effect following administration of large amounts of the drug is short-term suppression of hypothalamic-pituitary-adrenal (HPA) function. No special first aid measures are required in this case. Treatment with BECLOSP should be continued at the recommended doses. HPA function is restored in one or two days.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Nasal decongestant for topical use-Corticosteroids
ATC code: R01AD01

Mechanism of action
Beclomethasone dipropionate (BDP) is a corticosteroid for topical use characterized by potent anti-inflammatory and vasoconstrictor effects on the mucous membranes of the nasal passages.
BDP is a prodrug with weak binding affinity for glucocorticoid receptors.
It is hydrolyzed by esterase enzymes to its active metabolite beclomethasone-17-monopropionate (B-17-MP), which has a high topical anti-inflammatory effect.

Pharmacodynamic effects
Beclomethasone 17,21-dipropionate (BDP) exerts potent anti-inflammatory and vasoconstrictor effects following topical application. When taken before an allergen attack, beclomethasone dipropionate provides a protective therapeutic basis for hay fever. After regular use, BDP continues to prevent the recurrence of allergy symptoms by desensitizing the nasal membrane.

5.2. Pharmacokinetic properties
General Properties
Absorption
Following intranasal administration of BDP, plasma concentrations of its active metabolite B-17-MP were measured and systemic absorption was evaluated both with and without the administration of activated charcoal. In the absence of activated charcoal administration, the absolute bioavailability of this active metabolite following intranasal administration was 44%. This is due to absorption of the ingested fraction rather than nasal absorption. The dose absorbed from the nasal mucosa following intranasal administration is less than 1%. The plasma concentration of B-17-MP is almost entirely the result of metabolism of BDP absorbed from the ingested dose.

Systemic absorption was evaluated by measuring plasma concentrations of the active metabolite B-17-MP following oral administration of BDP. The absolute bioavailability following oral administration is 41%. Following oral dosing, B-17-MP is absorbed slowly and reaches peak plasma concentrations after 3-5 hours.

Distribution
In constant medium, tissue distribution is moderate for BDP (201) but slightly higher for B-17-MP (4241). Binding to plasma proteins is higher (87%).

Biotransformation
BDP is rapidly cleared from the circulation following oral and intranasal dosing and plasma concentrations are not measurable (<50 picogram/mL). Metabolism of the drug is assisted by esterase enzymes found in many tissues. The major product of BDP metabolism is the active metabolite beclomethasone-17-monopropionate (B-17-MP). Minor active metabolites

beclomethasone-21-monopropionate (B-21-MP) and hydroxylated beclomethasone (BOH) are formed, but very little of these enter the systemic circulation.

Elimination

Elimination of BDP and B-17-MP is characterized by terminal elimination half-lives of 0.5 and 2.7 hours with high plasma clearance. Following oral administration of BDP, approximately 60% is excreted in the feces as free and conjugated polar metabolites within 96 hours. Approximately 12% is excreted in the urine as free and conjugated polar metabolites. Renal clearance of BDP is negligible.

5.3. Preclinical safety data

No clinically relevant findings were observed in preclinical studies.

Preclinical data indicate that benzalkonium chloride may have toxic effects on the cilia vibrations of the nasal mucosa epithelium, such as irreversible immobilization, depending on concentration and duration, and therefore histopathological changes in the nasal mucosa may occur.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Polysorbate 20
Glucose monohydrate
Microcrystalline cellulose and carmellose sodium
Benzalkonium chloride 50% aqueous solution
Phenylethyl alcohol
Hydrochloric acid
Distilled water

6.2. Incompatibilities

Not reported.

6.3. Shelf life

24 months.
The expiration date indicated is the date on the unopened and properly stored package.

6.4. Special precautions for storage

BECLOSP should be stored at room temperature below 25°C and in its packaging.

6.5. Nature and contents of the package

The primary packaging material is an amber colored PET bottle with a scale pump and nasal applicator for 200 or 120 applications and the secondary packaging is a protective cap and protective ring. It is supplied in a cardboard box with 1 bottle and instructions for use.

6.6. Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. This medicinal product may pose a risk to the aquatic environment.

7. MARKETING AUTHORIZATION HOLDER

Deva Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. 34303 No:1
Küçükçekmece/İSTANBUL
Phone: +90 212 692 92 92
Fax: +90 212 697 00 24
E-mail: deva@devaholding.com.tr

8. MARKETING AUTHORIZATION NUMBER

2019/231

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 24.04.2019
Date of last renewal:

10. DATE OF REVISION OF THE TEXT