SCHEDULING STATUS: S2

PROPRIETARY NAME AND DOSAGE FORM:

ZILFONE NASAL SPRAY

COMPOSITION:

Active ingredient:

Zilfone Nasal Spray is a metered-dose, manual pump spray unit containing a suspension of mometasone furoate. Each metered dose pump actuation of Zilfone Nasal Spray delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 µg mometasone furoate.

Excipients:

Citric acid monohydrate, glycerol, microcrystalline cellulose and carmellose sodium (Avicel RC-591), polysorbate 80, sodium citrate dihydrate and water for injection.

Preservative:

Benzalkonium chloride 0,02 % *m/m*.

PHARMACOLOGICAL CLASSIFICATION:

A.21.5.1 Corticosteroids and analogues

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Mometasone furoate is a topical glucocorticosteroid with local anti-inflammatory properties.

It is likely that much of the mechanism for the anti-allergic and anti-inflammatory effects of mometasone furoate lies in its ability to inhibit the release of mediators of allergic reactions. Mometasone furoate significantly inhibits the release of leukotrienes from leucocytes of allergic patients. In cell culture, mometasone furoate demonstrated high potency in inhibition of synthesis and release of IL-1, IL-5, IL-6 and TNFα; it is also a potent inhibitor of leukotriene production. In addition, it is an extremely potent inhibitor of the production of the Th2 cytokines, IL-4 and IL-5, from human CD4+ T-cells.

Pharmacokinetic properties:

Absorption:

Mometasone furoate, administered as an aqueous nasal spray, has a systemic bioavailability of < 1 % in plasma, using a sensitive assay with a lower quantitation limit of 0,25 pg/mℓ.

Distribution:

Not applicable as mometasone is poorly absorbed via the nasal route.

Biotransformation:

The small amount that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism. Mometasone furoate is mainly metabolised by the cytochrome P450 isoenzyme CYP3A4.

Elimination:

Terminal elimination half-life is about 5 hours. The absorbed mometasone furoate is extensively metabolised and the metabolites are excreted in urine and bile.

INDICATIONS:

ZILFONE NASAL SPRAY is indicated for use in adults, adolescents and children between the ages of 2 and 11 years to treat the symptoms of seasonal allergic or perennial allergic rhinitis.
In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with ZILFONE NASAL SPRAY is recommended prior to the anticipated start of pollen season.

CONTRAINDICATIONS:

Hypersensitivity to mometasone furoate or any of the excipients of ZILFONE NASAL SPRAY (see “COMPOSITION”).
Pregnancy and lactation (see “PREGNANCY AND LACTATION”).
Children under 2 years, as safety and efficacy have not been demonstrated.
Presence of untreated localised infection involving the nasal mucosa, such as herpes simplex (see “WARNINGS AND SPECIAL PRECAUTIONS”).
Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal surgery or trauma should not use a nasal corticosteroid until healing has occurred (see “WARNINGS AND SPECIAL PRECAUTIONS”).

WARNINGS AND SPECIAL PRECAUTIONS:

Patients receiving corticosteroids who are potentially immunosuppressed should be warned of the risk of exposure to certain infections (e.g. chickenpox, measles) and of the importance of obtaining medical advice if such exposure occurs.

ZILFONE NASAL SPRAY should not be used in the presence of untreated localised infection involving the nasal mucosa (see “CONTRAINDICATIONS”).
Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal surgery or trauma should not use a nasal corticosteroid until healing has occurred (see “CONTRAINDICATIONS”).

Following 12 months of treatment with mometasone in a study of patients with perennial rhinitis, there was no evidence of atrophy of the nasal mucosa; also, mometasone furoate tended to reverse the nasal mucosa closer to a normal histological mucosa.
Nevertheless, patients using ZILFONE NASAL SPRAY over several months or longer should be examined periodically for possible changes in the nasal mucosa. If localised fungal infection of the nose or pharynx develops, discontinuation of ZILFONE NASAL SPRAY or appropriate treatment may be

required. Persistence of nasopharyngeal irritation may be an indication for discontinuing ZILFONE NASAL SPRAY.

ZILFONE NASAL SPRAY is not recommended in case of nasal septum perforation.

ZILFONE NASAL SPRAY should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections or ocular herpes simplex.

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.

Large doses of corticosteroids, or of corticotropin, may produce Cushingoid symptoms typical of hyperactivity of the adrenal cortex, with moon-face, sometimes with hirsutism, buffalo hump, flushing, increased bruising, ecchymoses, striae, and acne.

Patients who are transferred from long-term administration of systemically active corticosteroids to ZILFONE NASAL SPRAY require careful attention. Systemic corticosteroid withdrawal in such patients may result in adrenal insufficiency for a number of months until recovery of hypothalamic-pituitary-adrenal (HPA) axis function. If these patients exhibit signs and symptoms of adrenal insufficiency, systemic corticosteroid administration should be resumed and other modes of therapy and appropriate measures instituted.
The negative feedback effects of glucocorticoids on the hypothalamic-pituitary-adrenal (HPA) axis may lead to adrenal atrophy, in some cases after therapy for as little as 7 days. This produces secondary adrenocortical insufficiency, which may become manifest after overly rapid withdrawal of treatment or be precipitated by some stress such as infection or trauma. Patients vary considerably in the degree and duration of adrenal suppression after a given course of corticosteroid, but adrenal atrophy may persist for months or years, and withdrawal should be gradual in those who have been treated for any length of time.

During transfer from systemic corticosteroids to ZILFONE NASAL SPRAY, some patients may experience symptoms of withdrawal from systemically active corticosteroids (e.g. joint and/or muscular pain, lassitude and depression initially) despite relief from nasal symptoms and will require encouragement to continue ZILFONE NASAL SPRAY therapy. Such transfer may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

Following the use of intranasal aerosolised corticosteroids, instances of nasal septum perforation or increased intraocular pressure have been reported.

Visual disturbance may be reported with systemic and topical (including intranasal, inhaled and intraocular) 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 of visual disturbances, 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.

The safety and efficacy of ZILFONE NASAL SPRAY has not been studied for use in the treatment of unilateral polyps, polyps associated with cystic fibrosis, or polyps that completely obstruct the nasal cavities.
Unilateral polyps that are unusual or irregular in appearance, especially if ulcerating or bleeding, should be further evaluated.

Although ZILFONE NASAL SPRAY will control the nasal symptoms in most patients, the concomitant use of appropriate additional therapy may provide additional relief of other symptoms, particularly ocular symptoms.

INTERACTIONS:
ZILFONE NASAL SPRAY has been administered concomitantly with loratadine with no apparent effect on plasma concentrations of loratadine or its major metabolite. Mometasone furoate plasma concentrations were not detectable.

Co-treatment with CYP3A inhibitors such as cimetidine, nelfinavir, ritonavir, clarithromycin, ketoconazole, fluconazole, erythromycin, verapamil, including cobicistat-containing medicine, are expected to increase the risk of systemic side effects.

PREGNANCY AND LACTATION:
The safety and efficacy of ZILFONE NASAL SPRAY in pregnant and lactating women have not been established (see “CONTRAINDICATIONS”).
High doses of corticosteroids given during pregnancy may cause foetal or neonatal adrenal suppression. Although the precise mechanism is uncertain, growth retardation may follow the use of even relatively small doses of corticosteroids in children. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for hypoadrenalism.

DOSAGE AND DIRECTIONS FOR USE:
After initial priming of the ZILFONE NASAL SPRAY (usually 10 actuations, until a uniform spray is observed), each actuation delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 mcg mometasone furoate. If the spray pump has not been used for 14 days or longer, it should be reprimed with 2 actuations, until a uniform spray is observed, before next use. No priming subsequent to the initial priming is required with regular use.

Shake container well before each use.

Seasonal or Perennial Allergic Rhinitis:

***Adults (including geriatric patients) and adolescents*:**

The usual recommended dose for prophylaxis and treatment is 2 sprays (50 mcg/spray) into each nostril once daily (total dose 200 mcg). Once symptoms are controlled, dose reduction to 1 spray into each nostril (total dose 100 mcg) may be effective in some patients for maintenance.

If symptoms are inadequately controlled, the dose may be increased to a maximum daily dose of 4 sprays into each nostril once daily (total dose 400 mcg).

Dose reduction is recommended following control of symptoms.

***Children between the ages of 2 and 11 years*:**

The usual recommended dose is 1 spray (50 mcg/ spray) into each nostril once daily (total dose 100 mcg).

Administration to young children should be aided by an adult.

SIDE EFFECTS:

Infections and infestations

Frequent: Pharyngitis, upper respiratory tract infection.

Immune system disorders

Frequency unknown: Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm and dyspnoea.

Psychiatric disorders

Frequency unknown: Mental and neurological disturbances.

Nervous system disorders

Frequency unknown: Dizziness, benign intracranial hypertension, headache.

Eye disorders

Frequency unknown: Conjunctivitis, dry eyes, increased intraocular pressure (glaucoma and cataracts), blurred vision.

Respiratory, thoracic and mediastinal disorders

Frequent: Epistaxis, nasal burning, nasal irritation, nasal ulceration, dryness inside nose.

Frequency unknown: Rhinitis, sinusitis, cough, nasal septum irritation, rhinorrhoea.

Gastrointestinal disorders

Less frequent: Disturbances of taste and smell, vomiting, throat irritation.

Frequency unknown: Nausea, acute pancreatitis.

Skin and subcutaneous tissue disorders

Frequency unknown: Skin rash, skin thinning, hyperhidrosis.

Musculoskeletal, connective tissue and bone disorders

Frequency unknown: Avascular necrosis of bone.

Reproductive system and breast disorders

Frequency unknown: Amenorrhoea.

General disorders and administrative site conditions

Frequent: Headache.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(see “SIDE EFFECTS”).

Because of the negligible (≤ 0,1 %) systemic bioavailability of ZILFONE NASAL SPRAY, overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage.

Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of hypopituitary-adrenal (HPA) axis function.

IDENTIFICATION:

Zilfone Nasal Spray: a white homogenous suspension.

PRESENTATION:

Zilfone Nasal Spray is packed into 20 mℓ white HDPE plastic bottle with a screw. A nasal spray pump with nasal actuator, protection cap (white) and dip tube is fixed to the bottle neck.

Bottles containing 17 g of nasal spray (120 metered sprays) or 18 g of nasal spray (140 metered sprays).

STORAGE INSTRUCTIONS:

Store at or below 25 °C, away from heat.

Do not freeze.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER:

46/21.5.1/0491.490

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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[1]Company Reg. No.: 1990/001979/07