

*For the use only of Registered Medical Practitioners or a Hospital or a Laboratory*

## **BETNESOL**

### **1. GENERIC NAME**

Betamethasone Sodium Phosphate Oral Drops

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each ml (approx. 20 drops) contains:

Betamethasone Sodium Phosphate IP equivalent to Betamethasone 0.5 mg

Colour: Sunset Yellow FCF

#### ***List of Excipients***

, Sodium Methyl Paraben, Sodium Propyl Paraben, Disodium Edetate, Sodium Phosphate, Phosphoric Acid, Sodium Hydroxide, Trisodium Phosphate, Propylene Glycol, Colour Sunset Yellow F.C.F and Purified water

### **3. DOSAGE FORM AND STRENGTH**

Solution for oral use

For information on strength(s) refer 2. *Qualitative and Quantitative Composition* above.

### **4. CLINICAL PARTICULARS**

#### **4.1 Therapeutic Indication**

A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are:-

- Bronchial asthma.
- Severe hypersensitivity reactions.
- Anaphylaxis.
- Rheumatoid arthritis.
- Systemic lupus erythematosus.
- Dermatomyositis.
- Mixed connective tissue disease (excluding systemic sclerosis).
- Polyarteritis nodosa.
- Inflammatory skin disorders, including pemphigus vulgaris.
- Bullous pemphigoid.
- Pyoderma gangrenosum.
- Minimal change nephrotic syndrome.
- Acute interstitial nephritis.
- Ulcerative colitis.
- Crohn's disease.
- Sarcoidosis.
- Rheumatic carditis.

- Haemolytic anaemia (autoimmune).
- Acute and lymphoblastic and chronic lymphocytic leukaemia.
- Malignant lymphoma.
- Multiple myeloma.
- Idiopathic thrombocytopenic purpura.
- Immunosuppression in transplantation.

## 4.2 Posology and Method of Administration

***BETNESOL Oral Drops has been specially formulated for children, but adults, particularly the elderly may prefer BETNESOL Oral Drops to BETNESOL Tablets.***

The lowest dosage that will produce an acceptable result should be used; when it is possible to reduce the dosage, this must be accomplished by stages. During prolonged therapy, dosage may need to be increased temporarily during periods of stress or in exacerbations of illness.

### ***Populations***

#### ***Adults***

The dose used will depend upon the disease, its severity, and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed.

***Short-term treatment:*** 2 to 3 mg daily for the first few days, subsequently reducing the daily dosage by 250 or 500 micrograms (0.25 or 0.5 mg) every two to five days, depending upon the response.

***Rheumatoid arthritis:*** 500 micrograms (0.5 mg) to 2 mg daily. For maintenance therapy the lowest effective dosage is used.

***Most other conditions:*** 1.5 to 5 mg daily for one to three weeks, then reducing to the minimum effective dosage. Larger doses may be needed for mixed connective tissue diseases and ulcerative colitis.

#### ***Children***

Fractions of the adult dosage may be used (e.g., 75% at 12 years, 50% at 7 years and 25% at 1 year) but clinical factors must be given due weight.

The dose used will depend upon the disease, its severity, and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed.

#### ***Short-term treatment:***

***At 12 years:*** 1.5 to 2.25 mg daily for the first few days, subsequently reducing the daily dosage by 187.5 or 375 micrograms (0.188 or 0.375 mg) every two to five days, depending upon the response.

***At 7 years:*** 1 to 1.5 mg daily for first few days, subsequently reducing the daily dosage by 125 or 250 micrograms (0.125 or 0.25 mg) every two to five days, depending upon the response.

*At 1 year:* 0.5 to 0.75 mg daily for the first few days, subsequently reducing the daily dosage by 62.5 or 125 micrograms (0.0625 or 0.125 mg) every two to five days, depending upon the response.

*Rheumatoid arthritis:*

*At 12 years:* 375 micrograms (0.375 mg) to 1.5 mg daily

*At 7 years:* 250 micrograms (0.25 mg) to 1 mg daily

*At 1 year:* 125 micrograms (0.125 mg) to 0.5 mg daily

For maintenance therapy the lowest effective dosage is used.

*Most other conditions:*

*At 12 years:* 1.125 to 3.75 mg daily for one to three weeks

*At 7 years:* 0.75 to 2.5 mg daily for one to three weeks

*At 1 year:* 0.375 to 1.125 mg daily for one to three weeks

Then reduce to the minimum effective dosage. Larger doses may be needed for mixed connective tissue diseases and ulcerative colitis.

### **4.3 Contraindications**

- Systemic infections unless specific anti-infective therapy is employed
- Live virus immunisation
- Hypersensitivity to any component of the preparation

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

Visual disturbance has been reported by patients using systemic and /or topical corticosteroids. If a patient has blurred vision or other visual disturbances, consider evaluation of possible causes which may include cataract, glaucoma or central serous chorioretinopathy.

Administration of corticosteroids may impair the ability to resist and counteract infection e.g., where there is a previous history of tuberculosis; in addition clinical signs and symptoms of infection are suppressed.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients without a definite history of chickenpox should be advised to avoid close contact with chickenpox or herpes zoster and, if exposed, they (or the parents of such children) should seek urgent medical attention. Passive immunisation with varicella / zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous three months. This should be given within ten days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.

Corticosteroid treatment is likely to reduce the response of the pituitary-adrenal axis to stress, and relative insufficiency may persist for up to a year after withdrawal of prolonged therapy.

Because of the possibility of fluid retention, care must be taken when corticosteroids are administered to patients with congestive heart failure.

Corticosteroids may worsen diabetes mellitus, osteoporosis, hypertension, glaucoma and epilepsy.

Care should be taken when there is a history of severe affective disorders (especially a previous history of steroid psychosis), previous steroid myopathy or peptic ulceration.

In patients with liver failure blood levels of corticosteroid may be increased, as with other drugs which are metabolised in the liver.

Systemic corticosteroids may cause growth retardation in infancy, childhood and adolescence. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimize suppression of the HPA axis and growth retardation consideration should be given to administration of a single dose on alternate days.

Treatment of elderly patients, particularly if long term, should be planned bearing in mind the more serious consequences of the common side effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, susceptibility to infection and thinning of the skin.

When treatment is to be discontinued, the dose should be reduced gradually over a period of several weeks or months depending on the dosage and duration of the therapy.

In rare cases reduction or withdrawal of oral corticosteroid therapy may unmask underlying eosinophilic conditions (e.g., Churg Strauss syndrome) in patients with asthma.

*BETNESOL* Oral Drops contains Colour Sunset Yellow F.C.F. which may cause allergic type reactions.

#### **4.5 Drug Interactions**

Corticosteroids may reduce the effects of anticholinesterases in myasthenia gravis, cholecystographic x-ray media, salicylates and non-steroidal anti-inflammatory agents.

The effect of corticosteroids may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin.

The dosage of concomitantly administered anti-coagulants may have to be altered (usually decreased).

Oestrogens may potentiate the effects of glucocorticoids and dosage adjustments may be required if oestrogens are added to or withdrawn from a stable dosage regimen.

Betamethasone is metabolised by CYP3A4 and co-administration with CYP3A inhibitors (e.g. ritonavir, cobicistat, itraconazole) is expected to increase the systemic concentration of betamethasone.

#### **4.6 Use in Special Populations**

The use of corticosteroids during human pregnancy and lactation requires that the benefits be weighed against the possible risks associated with the product or with any alternative therapy.

## ***Pregnancy***

There is insufficient evidence of safety in human pregnancy.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intrauterine growth retardation. The relevance of this finding to human beings has not been established, however, patients should avoid extensive use in pregnancy.

Hypoadrenalism may occur in the neonate.

## ***Lactation***

Corticosteroids are excreted in small amounts in breast milk and infants of mothers taking pharmacological doses of corticosteroids should be monitored carefully for signs of adrenal suppression.

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

None identified

### **4.8 Undesirable Effects**

Prolonged treatment with corticosteroids in high dosage is occasionally associated with subcapsular cataract, skin thinning, osteoporosis, and glaucoma. In addition, any of the features of hypercortisolism, such as suppression of the HPA axis, may occur.

Aseptic osteonecrosis, particularly of the femoral head, may occur after prolonged corticosteroid therapy or after repeated short courses involving high dosage.

Peptic ulceration may develop, or be aggravated.

In children, prolonged therapy may retard growth.

In patients on long term therapy fluid and electrolyte balance may be altered.

Other rare side effects which have been reported include benign intracranial hypertension and psychic instability.

### **4.9 Overdose**

Acute overdosage is very unlikely to occur, however in the case of chronic overdosage or misuse the features of hypercortisolism, may appear and in this situation the product should be discontinued slowly.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Mechanism of action and Pharmacodynamic Properties**

Corticosteroids exhibit anti-inflammatory, antipruritic, and vasoconstrictive properties. At the cellular level, corticosteroids induce peptides called lipocortins. Lipocortins antagonize phospholipase A<sub>2</sub>, an enzyme which causes the breakdown of leukocyte lysosomal membranes to release arachidonic acid. This action decreases the subsequent formation and release of endogenous inflammatory mediators including prostaglandins, kinins, histamine, liposomal enzymes and the complement system.

Early anti-inflammatory effects of topical corticosteroids include the inhibition of macrophage and leukocyte movement and activity in the inflamed area by reversing vascular dilation and permeability. Later inflammatory processes such as capillary production, collagen deposition, keloid (scar) formation also are inhibited by corticosteroids. Clinically, these actions correspond to decreased edema, erythema, pruritus, plaque formation and scaling of the affected skin.

### **5.2 Pharmacokinetic Properties**

Betamethasone is rapidly absorbed following an oral dose with peak effects occurring within 1-2 hours. Betamethasone that is systemically absorbed is quickly distributed into the kidneys, intestines, skin, liver, and muscle. Betamethasone binds weakly to plasma proteins, and only the unbound portion of a circulating dose is active. Corticosteroids distribute into the breast milk and cross the placenta. Systemic betamethasone is metabolized by CYP3A4 to inactive metabolites. These inactive metabolites, as well as a small portion of unchanged drug, are excreted in the urine. The biological half-life of betamethasone is 35 to 54 hours.

## **6. NONCLINICAL PROPERTIES**

No relevant text.

## **7. DESCRIPTION**

Solution for oral use

Each ml (approx. 20 drops) contains:

Betamethasone Sodium Phosphate IP equivalent to Betamethasone 0.5 mg

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### ***List of Excipients***

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## **8. PHARMACEUTICAL PARTICULARS**

### **8.1 Incompatibilities**

There are no relevant data available.

## 8.2 Shelf Life

The expiry date is indicated on the label and packaging.

## 8.3 Packaging Information

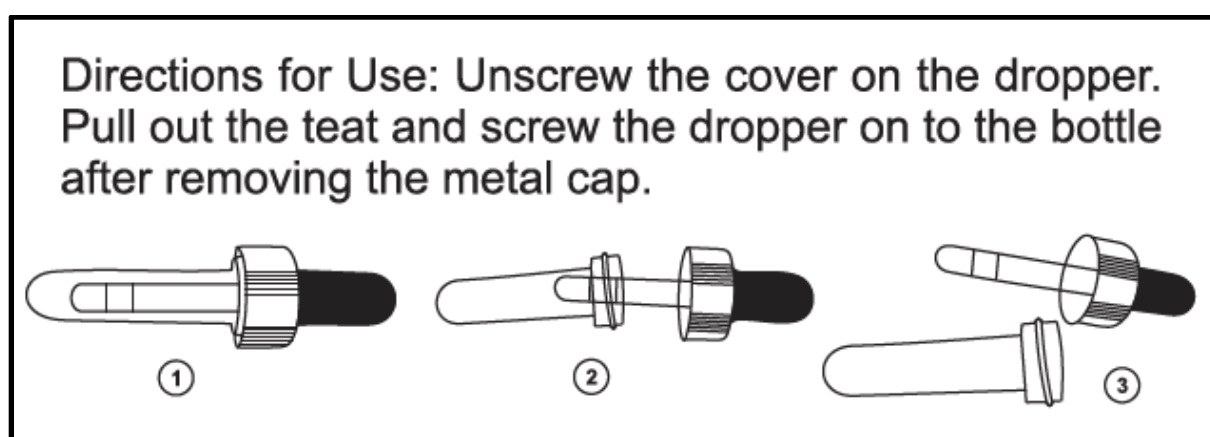
Bottle and a dropper with cover in a carton

## 8.4 Storage and Handling Instructions

Store in a well closed container at temperatures not exceeding 30°C. Protect from direct sunlight.

Keep out of reach of children.

To be used within one month of opening the bottle.



## 9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contraindications of *BETNESOL*. Patients (and/or patients' caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

## 10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

### For further information please contact:

GlaxoSmithKline Pharmaceuticals Limited,

### Registered Office:

Dr. Annie Besant Road, Worli

Mumbai 400 030, India.

## 11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

## **12. DATE OF REVISION**

22-NOV-2023

*Trade marks are owned by or licensed to the GSK group of companies.*

*Version: BET-OD/PI/IN/2023/01*

*Adapted from:*

*Betamethasone sodium phosphate GDS Version 08 dated 03 April 2018. Clinical Pharmacology - Betamethasone Monograph available from:*

<https://www.clinicalkey.com/pharmacology/monograph/64>