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 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 2000 micrograms (2 mg) daily. For maintenance therapy the lowest effective dosage is used.

Most other conditions: 1.5 mg 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 adverse reactions 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

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency. Frequencies are defined as: very common (≥1/10), common (>1/100 and <1/10), uncommon (>1/1,000 and <1/100), rare (>1/10,000 and <1/1,000), very rare (<1/10,000), and not known (cannot be estimated from the available data).

System Organ Class	Adverse reaction(s)	Frequency
Endocrine disorders	Prolonged treatment with corticosteroids in high dosage is associated with any of the features of hypercortisolism, such as suppression of the HPA axis. In children, prolonged therapy may retard growth.	Not known Not Known
Metabolism and nutrition disorders	Hypokalemia, hypokalemic paralysis. Altered fluid and electrolyte balance.	Very rare Not Known
Psychiatric disorders	Psychic instability.	Rare
Nervous system disorders	Benign intracranial hypertension.	Rare
Eye disorders	Prolonged treatment with corticosteroids in high dosage is associated with subcapsular cataract and glaucoma.	Not known

System Organ Class	Adverse reaction(s)	Frequency
Gastrointestinal disorders	Peptic ulceration may develop, or be aggravated.	Not known
Skin and subcutaneous tissue disorders	Prolonged treatment with corticosteroids in high dosage is associated with skin thinning.	Not known
Musculoskeletal and connective tissue disorders	Prolonged treatment with corticosteroids in high dosage is associated with osteoporosis. Aseptic osteonecrosis, particularly of the femoral head, may occur after prolonged corticosteroid therapy or after repeated short courses involving high dosage.	Not known Not known

4.9 Overdose

Symptoms and Signs

Acute overdosage is very unlikely to occur, however in the case of chronic overdosage or misuse the features of hypercortisolism (see *section 4.8 Undesirable Effects*), may appear and in this situation the product should be discontinued slowly (see *section 4.4 Special Warnings and Precautions for Use*).

Treatment

There is no specific treatment for an overdose of betamethasone sodium phosphate. If overdose occurs, the patient is to be treated supportively with appropriate monitoring as necessary. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

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_2, 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
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

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

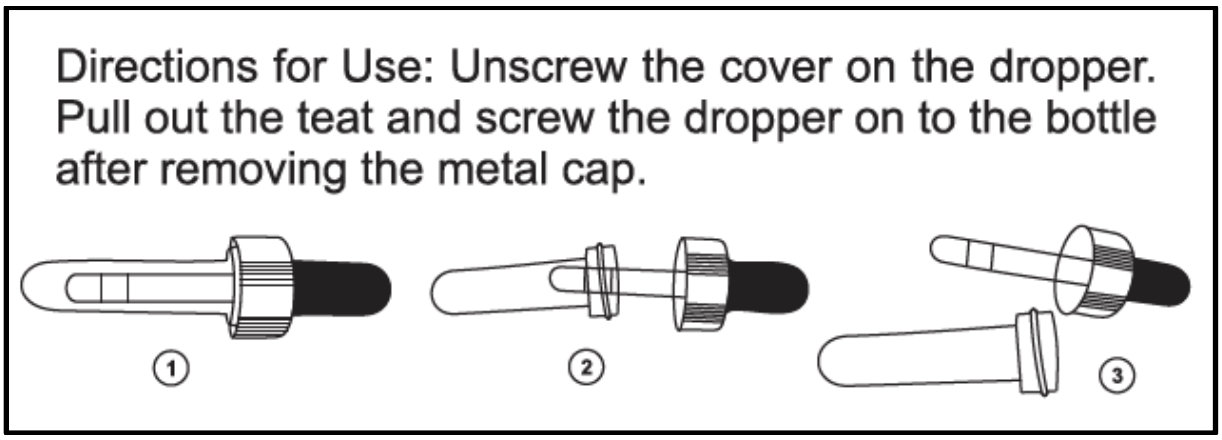
Bottle and a dropper with cover in a carton

8.4 Storage and Handling Instructions

Store in a well closed container at temperatures not exceeding 30ºC. 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.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

11-FEB-2025

Version: BET-OD/PI/IN/2025/01

Adapted from:

- *Betamethasone sodium phosphate GDS Version 09 dated 9 December 2024.*
- *Clinical Pharmacology - Betamethasone Monograph available from:* https://www.clinicalkey.com/pharmacology/monograph/64