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

BETNELAN TABLETS

Betamethasone Tablets I.P. 0.5mg

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:
Betamethasone I.P. 0.5 mg

PHARMACEUTICAL FORM

Uncoated Tablets

CLINICAL PARTICULARS

Therapeutic Indications

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, and 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.

Posology and Method of Administration

The lowest dosage that will produce an acceptable result should be used. When it is possible to reduce the dosage, this must be accomplished in 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.

Note: Betamethasone is also available as Betnesol Oral Drops where each ml (approx. 20 drops) contains Betamethasone 0.5 mg (as Betamethasone Sodium Phosphate).

Contraindications

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

Special Warnings and Special Precautions for Use

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 see 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 minimise 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.

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.

Interaction with Other Medicaments and Other Forms of Interaction

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.

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.

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.

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

Pregnancy and Lactation

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 steroids should be monitored carefully for signs of adrenal suppression.

Effects on Ability to Drive and Use Machines

None identified.

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 that have been reported include benign intracranial hypertension and pyschic instability.

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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Mechanism of action
Betamethasone is a synthetic analog of prednisolone which is more potent milligram per milligram than hydrocortisone.

Corticosteroids have multiple actions which produce antiinflammatory effects and result in their widespread use for treating diseases such as asthma. Historically, glucocorticoids were thought to decrease inflammation by stabilizing the lysosomes in neutrophils which prevented degranulation and the resulting inflammatory response. Additional research demonstrated that glucocorticoids also induce the antiinflammatory protein, lipocortin. This protein inhibits the enzyme phospholipase A2 which inhibits synthesis of prostaglandins and lipoxygenase products. Corticosteroids also bind to glucocorticoid receptors (GRs) located in the cytoplasm. After binding occurs, the activated GR moves from the cytoplasm to the nucleus where upregulation of antiinflammatory genes (eg, lipocortin, neutral endopeptidase, inhibitors of plasminogen activator) occurs. This effect results from binding of the GRs to glucocorticoid response elements (GREs). Corticosteroids also decrease the stability of selected messenger RNA molecules which alter gene transcription. Genes affected by this action include those involved in synthesis of collagenase, elastase, plasminogen activator, nitric oxide synthase, cyclooxygenase type II, cytokines, and chemokines.

During allergic reactions, four types of cytokines are believed to induce allergic cell recruitment. The cytokines, tumor necrosis factor-alpha and interleukine (IL)-1, nonspecifically activate the endothelium which promotes recruitment of neutrophils, eosinophils, mononuclear cells and basophils. Selective activation of the endothelium results from release of the cytokines, IL-4 and IL-13. These cytokines promote expression of vascular cell adhesion molecule-1 and binding of basophils, eosinophils, monocytes and lymphocytes

which have the leukocyte counterligand very late activation antigen-4. The third class of cytokines, IL-3, IL-5, granulocyte-macrophage colony-stimulating factor (GM-CSF), and interferon gamma, cause prolonged eosinophil survival, increased adhesion molecule expression, and increased eosinophil degranulation and movement across the endothelial barrier. The last class of cytokines, the chemokines, have chemotactic properties which induce cell migration and activate selected cell types. Corticosteroids are effective inhibitors of the described cytokines and thus reduce the inflammatory response elicited by these cytokines.

Pharmacokinetic Properties

Corticosteroids are, in general, readily absorbed from the gastrointestinal tract.

Corticosteroids are rapidly distributed to all body tissues. They cross the placenta to varying degrees and may be distributed in small amounts into breast milk.

Most corticosteroids in the circulation are extensively bound to plasma proteins, mainly to globulin and less so to albumin. The corticosteroid-binding globulin (transcortin) has high affinity but low binding capacity, while albumin has low affinity but large binding capacity. The synthetic corticosteroids are less extensively protein bound than hydrocortisone (cortisol). They also tend to have longer half-lives.

Corticosteroids are metabolised mainly in the liver but also in other tissues, and are excreted in the urine. The slower metabolism of the synthetic corticosteroids with their lower protein-binding affinity may account for their increased potency compared with the natural corticosteroids.

Clinical Studies

No relevant text.

Preclinical Safety Data

No relevant text.

PHARMACEUTICAL PARTICULARS

List of Excipients

Starch (Maize), Acacia Powder, Lactose, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Talc (Purified), Magnesium Stearate, Sodium Starch Glycollate, Purified Water.

Incompatibilities

No data available.

Shelf Life

The expiry date is indicated on the label and packaging.

Special Precautions for Storage

Keep in a cool dry place protected from direct sunlight.

Keep out of reach of children.

Nature and Specification of Container

Aluminium strips in a carton

Instructions for Use / Handling

No relevant information.

For further information please contact:
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