For the use of a Registered Medical Practitioner only

℞ Betamethasone Injection IP

Betzur*

COMPOSITION:

Each ml contains:

Betamethasone Sodium Phosphate IP

Eq. to Betamethasone ..... 4 mg

Phenol IP ..... 0.5% w/v
(As preservative)

Water for injections IP ..... q.s.

DOSAGE FORM

Liquid Injection

THERAPEUTIC INDICATIONS

It may be indicated in the following conditions:

Status asthmaticus and acute allergic reactions, including anaphylactic reactions to drugs. Betamethasone Injection supplements the action of adrenaline.

Severe shock arising from surgical or accidental trauma or overwhelming infection.

Acute adrenal crisis caused by abnormal stress in Addison's disease, Simmonds' disease, hypopituitarism following adrenalectomy, and when adrenocortical function has been suppressed by prolonged corticosteroid therapy.

Soft tissue lesions such as tennis elbow, tenosynovitis and bursitis.

NB. Betamethasone Injection does not replace other forms of therapy for the treatment of shock and status asthmaticus.

POSOLOGY AND METHOD OF ADMINISTRATION

Posology:

Systemic therapy in adults

4 to 20mg betamethasone (1 to 5ml) administered by slow intravenous injection over half to one minute. This does can be repeated three or four times in 24 hours, or as required, depending upon the condition being treated and the patient's response.

Alternatively, Betamethasone Injection may be given by intravenous infusion. The same dose can be given by deep intramuscular injection but the response is likely to be less rapid, especially in shock. This dose can be repeated three or four times in 24 hours depending upon the condition being treated and the patient's response.

Systemic therapy in paediatric population

Infants up to 1 year may be given 1mg betamethasone intravenously; children aged 1 to 5 years, 2mg; 6 to 12 years, 4mg (1ml). This dose can be repeated three or four times in 24 hours, depending upon the condition being treated and the patient's response.

Method of administration:

Betamethasone Injection may be administered by slow intravenous injection, deep intramuscular injection or subconjunctival injection. Alternatively, Betamethasone Injection may be given by intravenous infusion. Local injections of Betamethasone Injection may be used when treating soft tissue lesions.

The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal (HPA) axis suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment.

Other routes

Local injections of 4 to 8mg Betamethasone Injection may be used when treating soft tissue lesions in adults; children may require smaller doses. This dose can be repeated on two or three occasions depending upon the patient's response.

Betamethasone Injection has also been administered sub-conjunctivally as a single injection of 0.5 to 1 ml.

Intrathecal use is not recommended.

CONTRA-INDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

Systemic infections, unless specific anti-infective therapy is employed.

Betamethasone Injection should not be injected directly into tendons.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Undesirable effects may be minimised by using the lowest effective dose for the minimum period and by administering the daily requirement as a single morning dose or whenever possible as a single morning dose on alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity.

Caution is advised with the use of corticosteroids in patients who have suffered a recent myocardial infarction because of the risk of myocardial rupture.

Caution is advised on the use of corticosteroids in patients with hypothyroidism or myasthenia gravis.

Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they 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 3 months; this should be given within 10 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.

Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

Patients should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.

Corticosteroids should not be used for management of head injury or stroke because it is unlikely to be of benefit and may even be harmful.

In the treatment of cerebral oedema due to tumour, gastrointestinal bleeding may occur and stool examination may be helpful in diagnosis.

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids.

Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Adrenal suppression:

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment.

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1mg betamethasone or equivalent) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as a dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 1mg betamethasone is reached, dose reduction should be slower to allow the HPA-axis to recover.

During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Special Precautions

Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

A. Osteoporosis (post-menopausal females are particularly at risk).
B. Hypertension or congestive heart failure.
C. Existing or previous history of severe affective disorders (especially previous steroid psychosis).
D. Diabetes mellitus (or a family history of diabetes).
E. History of, or active, tuberculosis.
F. Glaucoma (or a family history of glaucoma).
G. Previous corticosteroid-induced myopathy.
H. Liver failure – blood levels of corticosteroid may be increased, as with other drugs which are metabolised in the liver.
I. Renal insufficiency.
J. Epilepsy.
K. History of, or active, peptic ulceration.
L. Herpes simplex keratitis.
M. Diverticulitis.
N. Thromboembolic tendencies.

Patients should carry 'steroid treatment' cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.

Visual disturbance

Visual disturbance may be reported with systemic and topical 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 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.

Paediatric population

Caution is advised in children as they are more susceptible to systemic toxicity from betamethasone.

Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. 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.

Elderly

The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

DRUG INTERACTIONS

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

Rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, aminoglutethimide and ephedrine enhance the metabolism of corticosteroids; thus the corticosteroid therapeutic effect may be reduced.

The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

The effect of corticosteroids may be reduced for 3-4 days after mifepristone.

The growth promoting effect of somatropin may be inhibited by corticosteroids.

An increase in the incidence of gastrointestinal bleeding may occur if NSAIDS are taken concomitantly with corticosteroids.

Corticosteroids may antagonise the effects of neuromuscular blocking drugs such as vecuronium.

Concurrent use of corticosteroids and fluoroquinolones may result in increased risk of tendon rupture.

Concomitant use of betamethasone with quetiapine may result in the increased metabolism of quetiapine and, depending on the clinical response, a higher dose of quetiapine may need to be considered.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

USE IN SPECIAL POPULATIONS

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs, however, betamethasone readily crosses the placenta. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. Myocardial hypertrophy and gastroesophageal reflux have been reported in association with in-utero exposure to betamethasone.

Breast-feeding

Corticosteroids may pass into breast milk, although no data are available for betamethasone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

UNDESIRABLE EFFECTS

The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal (HPA) axis suppression, correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment.

Not known: frequency cannot be estimated from the available data.

System organ class	Frequency	Undesirable effects
Infections and infestations	Not known	Increased susceptibility to and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis
Endocrine disorders	Not known	Suppression of the HPA axis, growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea.
Metabolism and nutrition disorders	Not known	Cushingoid facies, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy*
Psychiatric disorders	Common	A wide range of psychiatric reactions**
Eye disorders	Not known	Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases Vision, blurred
Cardiac disorders	Not known	Myocardial rupture following recent myocardial infarction
Gastrointestinal disorders	Not known	Abdominal distension, oesophageal ulceration, nausea, dyspepsia, peptic ulceration with perforation and haemorrhage, acute pancreatitis, candidiasis
Skin and subcutaneous tissue disorders	Not known	Impaired healing, skin atrophy, bruising, telangiectasia, striae, acne, Stevens-Johnson syndrome.
Musculoskeletal and connective tissue disorders	Not known	Osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, proximal myopathy
General disorders and administration site conditions	Not known	Hypersensitivity including anaphylaxis has been reported. Leucocytosis, Thrombo-embolism, Malaise, Hiccups

* Negative protein, nitrogen and calcium balance. Increased appetite. Hyperhidrosis. Increased high-density lipoprotein and low – density lipoprotein concentration in the blood. Fluid and electrolyte disturbance (Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis)

** Including affective disorder (such as irritable, euphoric, depressed and labile mood and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to the 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown. Psychological dependence. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal. Aggravation of epilepsy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine.

Kindly report any suspected adverse reactions to pharmavigil@jbpharma.com

OVERDOSE

Should over dosage occur, the possibility of adrenal suppression should be minimised by a gradual reduction of dosage over a period of time.

The patient may need support during any further trauma.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Betamethasone sodium phosphate in an active corticosteroid with topical anti-inflammatory activity.

ATC code: HO2A B01

Betamethasone is a glucocorticoid which is about eight to ten times as active as prednisolone on a weight-for-weight basis.

Pharmacokinetic properties

Corticosteroids are bound to plasma protein in varying degrees.

Biotransformation

Corticosteroids are metabolised primarily by the liver.

Elimination

Corticosteroids are excreted by the kidneys.

Nonclinical Toxicology

None stated.

INCOMPATIBLITIES

No incompatibilities have been identified.

PACKAGING INFORMATION

1ml clear Ampoules in blister pack in carton.

STORAGE AND HANDLING INSTRUCTIONS

Store protected from light at a temperature not exceeding 30^0 C.

Marketed by :
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road,
Worli, Mumbai - 400 030. India.
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DATE OF REVISION
April 2023

Note: This prescribing information is applicable for India Market only