

# DBL™ Dexamethasone Sodium Phosphate

## NAME OF THE MEDICINE

Dexamethasone Phosphate (as sodium)

## PRESENTATION

Each millilitre of solution contains Dexamethasone Phosphate (as sodium) equivalent to 4 mg or 24 mg of Dexamethasone Phosphate, Sodium Citrate 10 mg and Creatinine 8 mg. The pH of the solution is adjusted using sodium hydroxide and/or hydrochloric acid. Vials of Dexamethasone Phosphate 24 mg/mL also contain Disodium Edetate 0.5 mg/mL. No preservatives or antioxidant are present.

## USES

### Actions

Dexamethasone is a synthetic corticosteroid (glucocorticoid). As such its main actions may be grouped as follows:

**Anti-inflammatory and Immunological Actions:** Glucocorticoids prevent the development of the inflammatory response, ie. redness, swelling, tenderness. They also inhibit capillary dilation and phagocytosis and appear to prevent the hypersensitivity responses which occur after antigen-antibody reactions.

**Pharmacological Actions:** The principal action of dexamethasone is on gluconeogenesis, glycogen deposition and protein and calcium metabolism, together with inhibition of corticotrophin secretion. Glucocorticoids also influence the mobilisation, oxidation, synthesis and storage of fats. Except for its use in the treatment of adrenal insufficiency it does not cure disease but it is used rather to treat disease symptoms because of its pharmacological properties, ie. anti-inflammatory and anti-allergic actions.

### Pharmacokinetics

Intramuscular injections of dexamethasone phosphate give maximum plasma concentrations of dexamethasone at 1 hour. The biological half-life of dexamethasone is about 190 minutes.

In circulation, small amounts of dexamethasone are bound to plasma proteins. Dexamethasone penetrates into tissue fluids and cerebrospinal fluids. Metabolism of the drug takes place in the kidney and liver and excretion is via the urine.

### Indications

Dexamethasone is clinically indicated in the following situations.

## Replacement Therapy - Adrenocortical Insufficiency

Dexamethasone has predominantly glucocorticoid activity and therefore is not a complete replacement therapy. It should be supplemented with salt and or a mineralocorticoid. When so supplemented dexamethasone is indicated in:

- Acute adrenocortical insufficiency - Addison's disease, bilateral adrenalectomy.
- Relative adrenocortical insufficiency - Prolonged administration of adrenocortical steroids can produce dormancy of the adrenal cortex. The reduced secretory capacity gives rise to a state of relative adrenocortical insufficiency which persists for a varying length of time after therapy is discontinued. Should a patient be subjected to sudden stress during this period of reduced secretion (for up to two years after therapy has ceased) the steroid output may not be adequate. Steroid therapy should therefore be reinstated to help cope with stress such as that associated with surgery, trauma, burns, or severe infections where specific antibiotic therapy is available.
- Primary and secondary adrenocortical insufficiency.

## Disease Therapy

### Collagen Diseases:

- Systemic lupus erythematosus
- Polyarteritis nodosa
- Dermatomyositis
- Giant cell arteritis
- Adjunctive therapy for short term administration during an acute episode or exacerbation of the above four diseases
- Acute rheumatic carditis - during an exacerbation or as maintenance therapy

### Pulmonary Disorders:

- Status asthmaticus
- Chronic asthma
- Sarcoidosis
- Respiratory insufficiency

### Blood Disorders:

- Leukaemia.
- Idiopathic thrombocytopenic purpura in adults.
- Acquired (autoimmune) haemolytic anaemia.

Rheumatic Diseases:

- Rheumatoid arthritis
- Osteoarthritis
- Adjunctive therapy for short term administration during an acute episode or exacerbation of Rheumatoid arthritis or Osteoarthritis

Skin Diseases:

- Psoriasis
- Erythema multiforme
- Pemphigus
- Neutrophilic dermatitis
- Localized neurodermatitis
- Exfoliative dermatitis
- Sarcoidosis of skin
- Severe seborrhoeic dermatitis
- Contact dermatitis

Gastrointestinal Disorders:

- Ulcerative colitis
- Regional enteritis

Oedema:

- Cerebral oedema - associated with primary or metastatic brain tumours, neurosurgery, stroke
- Oedema associated with acute non-infectious laryngospasm (or laryngitis)

Eye Disorders:

- Allergic conjunctivitis
- Keratitis.
- Allergic corneal marginal ulcers
- Chorioretinitis.
- Optic neuritis
- Anterior ischaemic optic neuropathy

#### Neoplastic States:

- Cerebral neoplasms
- Hypercalcaemia associated with cancer
- Leukaemias and lymphomas in adults
- Acute Leukaemia in children

#### Endocrine Disorders:

- Adrenal insufficiency

#### Preoperative and Post Operative Support

Dexamethasone may be used in any surgical procedure when the adrenocortical reserve is doubtful. This includes the treatment of shock due to excessive blood loss during surgery.

#### Shock

Dexamethasone may be used as an adjunct in the treatment of shock. Vials of Dexamethasone Phosphate 120 mg/5 mL are specifically designed for shock therapy where high pharmacological doses may be needed. Dexamethasone should not be used as a substitute for normal shock therapy.

### **DOSAGE AND ADMINISTRATION**

Dosage of dexamethasone phosphate (as sodium) is usually expressed in terms of dexamethasone phosphate.

#### **Intravenous and Intramuscular Administrations**

Note: The 120 mg in 5 mL presentation is for I.V. use only.

I.M. or I.V. dosage of dexamethasone phosphate is variable, depending on the condition being treated. It usually ranges from 0.5 - 24 mg daily. The duration of therapy is dependent on the clinical response of the patient and as soon as improvement is indicated, the dosage should be adjusted to the minimum required to maintain the desired clinical response. Withdrawal of the drug on completion of therapy should be gradual.

#### Shock

A single I.V. injection of 2 to 6 mg/kg bodyweight which may be repeated in 2-6 hours if shock persists. High-dose therapy should be continued only until the patient's condition has stabilized and usually for no longer than 48-72 hours.

An alternative regime of 20 mg by I.V. injection initially followed by continuous I.V. infusion of 3 mg/kg bodyweight per 24 hours has been suggested. If required for I.V.

infusion, dexamethasone phosphate 120 mg/5 mL may be diluted with glucose or sodium chloride injection.

To avoid microbial contamination hazards, infusion should be commenced as soon as practicable after preparation of the mixture. Infusion should be completed within 24 hours of preparation of the solution and any residue discarded.

**Warning:**

Further diluted solutions which are not clear or show evidence of particulate matter contamination should be discarded.

**Cerebral Oedema**

An initial dose of 10 mg I.V. followed by 4 mg I.M. every 6 hours until the symptoms of oedema subside (usually after 12 to 24 hours). After 2 to 4 days the dosage should be reduced and gradually stopped over a period of 5 to 7 days. Patients with cerebral malignancy may require maintenance therapy with doses of 2 mg I.M. or I.V. 2-3 times daily.

**Life-Threatening Cerebral Oedema**

**High Dose Schedule:**

	<u>Adults</u>	<u>Children &gt; 35kg</u>	<u>Children &lt; 35kg</u>
Initial Dose	50mg IV	25mg IV	20mg IV
1st day	8mg IV every 2 hrs	4mg IV every 2 hrs	4mg IV every 3 hrs
2nd day	8mg IV every 2 hrs	4mg IV every 2 hrs	4mg IV every 3 hrs
3rd day	8mg IV every 2 hrs	4mg IV every 2 hrs	4mg IV every 3 hrs
4th day	4mg IV every 2 hrs	4mg IV every 4 hrs	4mg IV every 6 hrs
5th-8th day	4mg IV every 4 hrs	4mg IV every 6 hrs	2mg IV every 6 hrs
After 8 days	Decrease by daily reduction of 4mg	Decrease by daily reduction of 2mg	Decrease by daily reduction of 1mg

NOTE: The intravenous and intramuscular routes of administration of DBL™ Dexamethasone Sodium Phosphate Injection should only be used where acute illness or life-threatening situations exist. Oral therapy should be substituted as soon as possible.

## **Intra-Synovial & Soft Tissue Injections**

Dosage varies with the degree of inflammation and the size and location of the affected area. Injections may be repeated from once every 3-5 days (eg. for bursae) to once every 2-3 weeks (for joints).

<i>Site of injection</i>	<i>Dosage</i>
Large Joints	2mg to 4mg
Small Joints	800 microgram to 1mg
Bursae	2mg to 3mg
Tendon Sheaths	400 microgram to 1mg
Soft tissue Infiltration	2mg to 6mg
Ganglia	1mg to 2mg

## **CONTRAINDICATIONS**

Unless considered life-saving, systemic administration of dexamethasone is contraindicated in systemic viral and fungal infections and in patients with peptic ulcer, osteoporosis and psychoses. Dexamethasone is also contraindicated in patients who are hypersensitive to the drug or any component of the injection.

## **WARNINGS AND PRECAUTIONS**

Patients who have received high or prolonged doses of corticosteroids should be given supplementary corticosteroids to overcome periods of stress caused by anaesthesia, surgery or trauma.

Long term treatment should not be abruptly discontinued.

Use only with extreme caution in patients with diabetes mellitus, infectious diseases, congestive heart failure, chronic renal failure, diverticulitis, hypertension, keratitis, epilepsy and in elderly persons.

Intra-articular injection of a corticosteroids may produce systemic as well as local effects.

Appropriate examination of any joint fluid present is necessary to exclude a septic process.

Local injection of a steroid into an infected site is to be avoided.

Corticosteroids should not be injected into unstable joints.

Patients should be impressed strongly with the importance of not overusing joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

Patients should not be vaccinated against smallpox while receiving corticosteroid therapy.

## **Pregnancy and Lactation**

### **Use in Pregnancy**

Category C: In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations). These findings do not seem to be relevant to humans. Reduced placental and birth weight have been recorded in animals and humans after long-term treatment. Since the possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the fetus when prescribing corticosteroids. However, the short-term use of antepartum corticosteroids for the prevention of respiratory distress syndrome, when warranted, does not seem to pose a risk.

## **ADVERSE EFFECTS**

Except for allergy the adverse effects listed have been associated with prolonged therapy and/or high doses.

### **Adrenal Suppression**

### **Allergy**

### **Blood/Vascular Disorders:**

- Thromboembolism
- Polymorphonuclear leucocytosis
- Neuropathy
- Vasculitis
- Development of Diabetes Mellitus

### **Effects on Bones and Joints:**

- Osteoporosis
- Arthropathy
- Osteonecrosis of femoral and/or humeral heads (aseptic or avascular necrosis)

### **Effects on Eyes:**

- Glaucoma
- Cataract

- Exophthalmos

Effects on Growth:

- Stunting of growth in children

Effects on Heart:

- Impaired myocardial contractility (prolonged treatment)

Effects on Muscle:

- Muscular atrophy

Effects on Skin:

- Impaired wound healing
- Allergic dermatitis
- Urticaria
- Erythema
- Thin fragile skin

Effects on Gastrointestinal System:

- Peptic ulcer
- Pancreatitis

Mental Effects:

- Euphoric side effects
- Headache
- Convulsion

Metabolic Effects:

- Electrolyte imbalance (retention of sodium and water with oedema and hypertension)
- Nitrogen depletion
- Hyperglycaemia



## INTERACTIONS

Concurrent administration of barbiturates, phenylbutazone, phenytoin or rifampicin may reduce the effects of corticosteroids. The action of anticoagulants may also be reduced by corticosteroids. Excessive potassium loss may occur if corticosteroids are administered concurrently with a potassium-depleting diuretic such as the thiazides or frusemide.

## OVERDOSAGE

### Symptoms

Reports of acute toxicity and/or deaths following overdose with glucocorticoids are rare. Exaggeration of corticosteroid related adverse effects may occur including hypertension, oedema, peptic ulceration, hyperglycaemia and altered mental state. Anaphylactic or hypersensitivity reactions may occur.

### Treatment

No antidote is available. Treatment of overdose is symptomatic. The dosage should be reduced or the drug withdrawn. Anaphylactic and hypersensitivity reactions may be treated with adrenaline (epinephrine), positive pressure artificial respiration, and aminophylline. The patient should be kept warm and quiet.

In case of overdose, immediately contact the Poisons Information Centre for advice (In Australia, call 13 11 26. In New Zealand, call 0800 764 766).

## PHARMACEUTICAL PRECAUTIONS

### Special Precautions for Storage

Store below 25°C. Protect from light.

## MEDICINE CLASSIFICATION

Prescription Medicine

## PACKAGE QUANTITIES

### Ampoules

<u>Strength</u>	<u>Packs</u>
4mg/mL	5's
4mg/mL	50's

## **Vials**

<u>Strength</u>	<u>Packs</u>
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8mg/2mL	5's
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8mg/2mL	50's
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120mg/5mL	1's
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## **NAME AND ADDRESS**

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## **DATE OF PREPARATION**

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