

1. NAME OF THE MEDICINAL PRODUCT

Dexamethasone Phosphate Panpharma 4 mg/mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution for injection contains 4.37 mg dexamethasone sodium phosphate equivalent to 4.00 mg of dexamethasone phosphate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dexamethasone Phosphate Panpharma is a sterile solution for injection. Clear and colourless to almost colourless solution, practically free from visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic 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 thrombocytopaenic 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
- Localised 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 and where high pharmacological doses are needed. Dexamethasone should not be used as a substitute for normal shock therapy.

4.2 Dose and method of administration

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

Intravenous and intramuscular administrations

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 medicine 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 stabilised 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.

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

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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:

	Adults	Children > 35 kg	Children < 35kg
Initial dose	50 mg IV	25 mg IV	20 mg IV
1 st day	8 mg IV every 2 hrs	4 mg IV every 2 hrs	4 mg IV every 3 hrs
2 nd day	8 mg IV every 2 hrs	4 mg IV every 2 hrs	4 mg IV every 3 hrs
3 rd day	8 mg IV every 2 hrs	4 mg IV every 2 hrs	4 mg IV every 3 hrs
4 th day	4 mg IV every 2 hrs	4 mg IV every 4 hrs	4 mg IV every 6 hrs
5 – 8 th day	4 mg IV every 4 hrs	4 mg IV every 6 hrs	2 mg IV every 6 hrs
After 8 days	Decrease by daily reduction of 4 mg	Decrease by daily reduction of 2 mg	Decrease by daily reduction of 1 mg

NOTE: The intravenous and intramuscular routes of administration of dexamethasone sodium phosphate should only be used where acute illness or life-threatening situations exist. Oral therapy should be substituted as soon as possible.

Intra-synovial and 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).

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

4.3 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 medicine or any component of the injection.

4.4 Special warnings and precautions for use

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 corticosteroid 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.

Metabolism and nutrition

Corticosteroids, including dexamethasone, can increase blood glucose, worsen pre-existing diabetes, and predispose those on long term corticosteroid therapy to diabetes mellitus; therefore corticosteroids should be used with caution in patients with, or a family history of, diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

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.

Because corticosteroids may increase blood glucose concentrations, dosage adjustments of anti-diabetic agents may be required.

4.6 Fertility, pregnancy and lactation

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 foetus 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.

Breast-feeding

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

Fertility

No data available.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable 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

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. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Symptoms

Reports of acute toxicity and/or deaths following overdosage 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 overdosage 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use. **ATC code:** H02A B02.

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, i.e. 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, i.e. anti-inflammatory and anti-allergic actions.

5.2 Pharmacokinetic properties

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.

5.3 Preclinical safety data

In animal studies, cleft palate was observed in rats, mice, hamsters, rabbits, dogs and primates; not in horses and sheep. In some cases these divergences were combined with defects of the central nervous system and of the heart. In primates, effects in the brain were seen after exposure. Moreover, intra-uterine growth can be delayed. All these effects were seen at high dosages.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Creatinine
- Sodium citrate
- Citric acid hydrate
- Sodium hydroxide
- Water for injections

6.2 Incompatibilities

Dexamethasone is physically incompatible with daunorubicin, doxorubicin, vancomycin, diphenhydramine (with lorazepam and metoclopramide) and metaraminol bitartrate and should not be admixed with solutions containing these medicines. It is also incompatible with doxapram and glycopyrrolate in syringe and with ciprofloxacin, idarubicin and midazolam in Y-site injections (1:1 mixture).

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

Any unused portion should be discarded immediately after use.

6.5 Nature and contents of container

Packs of 5 or 10 x 1 ml ampoules.

Packs of 5 or 10 x 2 ml ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

When Dexamethasone phosphate is given by intravenous infusion, dextrose 5% in water and sodium chloride 0.9% have been recommended as diluents. The exact concentration of dexamethasone per infusion container should be determined by the desired dose, patient fluid intake and drip rate required.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription medicine.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

28 February 2019

10. DATE OF REVISION OF THE TEXT

29 January 2020

SUMMARY TABLE OF CHANGES

Section	Summary of new information
4.6	Information on breast-feeding added
5.3	Preclinical safety information added
6.2	Incompatibilities of dexamethasone with other medicines updated
6.3	Editorial change
6.4 and 6.6	Special precautions for disposal and handling updated