

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DBL™ Dexamethasone Sodium Phosphate Injection 4 mg/mL Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of solution contains dexamethasone sodium phosphate equivalent to 4 mg of dexamethasone phosphate.

The 4 mg/1 mL ampoule formulation contains sodium citrate and creatinine. No preservatives or antioxidants are present.

The 8 mg/2 mL vial formulation contains sodium citrate, disodium edetate and sodium sulfite anhydrous. No preservatives are present.

Excipient(s) with known effect

Vial

Sodium sulfite

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Dexamethasone phosphate (as sodium) is a white or slightly yellow, very hygroscopic, crystalline powder. It is odourless or has a slight odour of alcohol. Dexamethasone phosphate (as sodium) is soluble 1 in 2 of water, slightly soluble in alcohol, practically insoluble in chloroform and ether, and very slightly soluble in dioxane.

DBL Dexamethasone Sodium Phosphate Injection is a clear colourless solution, free from visible particulate matter.

The pH of the solutions is adjusted using sodium hydroxide and/or hydrochloric acid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy - adrenocortical insufficiency

Dexamethasone has predominantly glucocorticoid activity and therefore is not a complete replacement therapy in cases of adrenocortical insufficiency. Dexamethasone should be supplemented with salt and/or a mineralocorticoid, such as deoxycorticosterone. 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

Dexamethasone is indicated for therapy of the following diseases:

Collagen diseases: Systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis, giant cell arteritis, adjunctive therapy for short-term administration during an acute episode or exacerbation, 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, 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 or 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 postoperative 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. Dexamethasone should not be used as a substitute for normal shock therapy.

4.2 Dose and method of administration

Dose

Intravenous and intramuscular administration

Dosage requirements are variable and must be individualised on the basis of the disease being treated and patient response.

Intravenous or intramuscular dosage usually ranges from 0.5 to 24 mg of dexamethasone phosphate 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.

Parenteral dexamethasone is generally reserved for patients who are unable to take the drug orally, or for use in an emergency situation.

Shock (of haemorrhagic, traumatic or surgical origin)

The usual dose for the treatment of shock is 2 to 6 mg/kg bodyweight as a single intravenous injection. This may be repeated in 2 to 6 hours if shock persists.

An alternative regimen of 20 mg by intravenous injection initially, followed by continuous intravenous infusion of 3 mg/kg bodyweight per 24 hours, has been suggested. If required for intravenous infusion, dexamethasone phosphate may be diluted with glucose or sodium chloride injection.

High dose therapy should be continued only until the patient's condition has stabilised and usually for no longer than 48 to 72 hours.

To avoid microbial contamination hazards, infusion should be commenced as soon as practicable after preparation of the mixture and if storage is necessary, store solution at 2 to 8°C. 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 which show evidence of particulate matter contamination, should be discarded.

Cerebral oedema

The treatment schedule and route of administration should reflect the severity and aetiology of the cerebral oedema. Treatment needs to be tailored to the individual response. An initial dose of 10 mg intravenously followed by 4 mg intramuscularly 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 intramuscularly or intravenously 2 to 3 times daily.

High doses of dexamethasone may be used to initiate short-term intensive therapy for acute cerebral oedema. Following an initial high loading dose, the dose is scaled down over the 7 to 10 days period of intensive therapy, and subsequently reduced to zero over the next 7 to 10 days.

High Dose Schedule:

	<i>Adults</i>	<i>Children > 35 kg</i>	<i>Children < 35 kg</i>
Initial Dose	50 mg (mg) IV	25 mg (mg) IV	20 mg (mg) IV
1 st day	8 mg IV every 2 hours	4 mg IV every 2 hours	4 mg IV every 3 hours
2 nd day	8 mg IV every 2 hours	4 mg IV every 2 hours	4 mg IV every 3 hours
3 rd day	8 mg IV every 2 hours	4 mg IV every 2 hours	4 mg IV every 3 hours
4 th day	4 mg IV every 2 hours	4 mg IV every 4 hours	4 mg IV every 6 hours
5 th -8 th day	4 mg IV every 4 hours	4 mg IV every 6 hours	2 mg IV every 6 hours
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 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 to 5 days (e.g. for bursae) to once every 2 to 3 weeks (for joints). Frequent intra-articular injection may result in damage to joint tissues.

Site of Injection

Dosage

Large Joints	2 mg to 4 mg
Small Joints	800 micrograms to 1 mg
Bursae	2 mg to 3 mg
Tendon Sheaths	400 micrograms to 1 mg
Soft Tissue Infiltration	2 mg to 6 mg
Ganglia	1 mg to 2 mg

Method of Administration

DBL Dexamethasone Sodium Phosphate Injection may be administered intravenously or intramuscularly for systemic effect, or as an intra-synovial or soft tissue injection for local effect.

Dosage of dexamethasone sodium phosphate is usually expressed in terms of dexamethasone phosphate.

Contains no antimicrobial agent. For single patient use. Use once only and discard any residue.

4.3 Contraindications

Administration of dexamethasone is contraindicated in the following cases:

- Systemic fungal infections, or other systemic infections unless specific anti-infective therapy is given (see section 4.4);
- Hypersensitivity to dexamethasone or other corticosteroids or to any component of the injection;
- Administration of live virus vaccines (see section 4.4);
- In patients with myasthenia gravis, peptic ulcer, osteoporosis or psychoses;
- The 8 mg/2 mL vial formulation is contraindicated in patients with a known hypersensitivity to sulfites.

4.4 Special warnings and precautions for use

Corticosteroids may increase susceptibility to or mask the symptoms of infection, and therefore should be used with caution in patients with systemic infections. Chicken pox, measles and other infections can have a more serious or even fatal effect in non-immune children or adults on corticosteroids. Immunosuppression is most likely to occur in patients receiving longer term, high dose systemic corticosteroid treatment; however, patients receiving moderate doses for short periods, or low doses over a prolonged period, may also be at risk.

Corticosteroids should be administered with caution to patients with latent tuberculosis or tuberculin reactivity, as reactivation of the disease may occur. These patients should therefore undergo chemoprophylaxis during prolonged corticosteroid therapy.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Administration of live virus vaccines is contraindicated in individuals receiving immunosuppressive doses of corticosteroids (see section 4.3). The antibody response to other vaccines may be diminished. If inactivated viral or bacterial vaccines are administered to patients receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunisation procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Long-term treatment should not be abruptly discontinued, as too rapid withdrawal may lead to drug induced secondary adrenocortical insufficiency. This may be minimised by gradual dosage reduction. This type of relative insufficiency may persist for months after therapy is discontinued. Therefore, in any situation of stress occurring in that period (such as anaesthesia, surgery or trauma), corticosteroid doses may need to be increased or the therapy reinstated. Following prolonged therapy, withdrawal of corticosteroids may result in symptoms of the corticosteroid withdrawal syndrome, including fever, myalgia, arthralgia and malaise.

Dexamethasone should be used only with extreme caution in patients with diabetes mellitus or in those with a family history of diabetes, infectious diseases, congestive heart failure or recent myocardial infarction, chronic renal failure, diverticulitis, hypertension, keratitis, epilepsy

and/or seizure disorder, non-specific ulcerative colitis (if there is a probability of impending perforation, abscess or other pyogenic infection), fresh intestinal anastomoses, active or latent peptic ulcer, osteoporosis, myasthenia gravis receiving anticholinesterase therapy since corticosteroid use may decrease plasma anticholinesterase activity, or in elderly persons. Geriatric patients may be more likely to develop hypertension and osteoporosis as a result of corticosteroid therapy.

Corticosteroids should be used with caution in patients who have had a recent cardiac infarction, as there have been reports of an apparent association between the use of corticosteroids and left ventricular free wall rupture in these patients; in patients with a history of severe affective disorders particularly of steroid induced psychoses; patients with previous steroid myopathy, liver failure, renal insufficiency, glaucoma; patients with thromboembolic disorders, patients with Duchenne's muscular dystrophy since transient rhabdomyolysis and myoglobinuria have been reported following strenuous physical activity; Cushing's disease. Corticosteroids show an enhanced effect in patients with hypothyroidism or cirrhosis.

Intra-articular injection of 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. Frequent intra-articular injection may result in damage to joint tissues. Patients should be advised strongly of the importance of not overusing joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

Adrenocortical insufficiency

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration and duration of therapy.

Symptoms of adrenal insufficiency include: malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration.

During prolonged courses of corticosteroid therapy sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of fluid intake and output and daily weight records may give an early warning of fluid retention.

Acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly, therefore withdrawal of corticosteroids should always be gradual. A degree of adrenal insufficiency may persist for 6 to 12 months; therefore, in any situation of stress occurring during that period steroid therapy may need to be reinstated. Since mineralocorticoid secretion may be impaired treatment with salt and/or a mineralocorticoid may also be needed.

During prolonged therapy, any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage.

Anti-inflammatory/immunosuppressive effects and infection

Suppression of the inflammatory response and immune function increases 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 recognized when corticosteroids are used. The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

Chickenpox is of particular concern since this may be fatal in immunosuppressed patients. Patients 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 immunization is recommended for non-immune patients who do come into contact with chickenpox. If a diagnosis of chickenpox is confirmed the illness warrants specialist care and urgent treatment.

Live vaccines are contraindicated in individuals on high doses of corticosteroids and should be postponed until at least 3 months after stopping corticosteroid therapy.

Ocular effects

Prolonged use of corticosteroids may produce subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves.

Corticosteroids should only be initiated in patients with ocular herpes simplex with appropriate viral cover by ophthalmologists because of the risk of corneal scarring loss of vision and corneal perforation.

Psychiatric effects

Patients and/or carers should be warned that potentially severe psychiatric reactions may occur. Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients and/or carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected.

Particular care is required when considering the use of corticosteroids in patients with existing or previous history of severe affective disorders.

Psychic derangements range from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations.

Paediatric population

Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible and therefore long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, treatment should be limited to the minimum suppression of the hypothalamic-pituitary-adrenal axis and growth retardation, the growth and development of infants and children should be closely monitored. Treatment should be administered where possible as a single dose on alternate days.

Children are at special risk from raised intracranial pressure.

Hypertrophic cardiomyopathy was reported after administration of dexamethasone to prematurely born infants, therefore appropriate diagnostic evaluation and monitoring of cardiac function and structure should be performed.

Use in the elderly

Long-term use in the elderly should be planned bearing in mind the more serious consequences of the common side effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, hypokalaemia, susceptibility to infection and thinning of the skin. Close medical supervision is required to avoid life-threatening reactions.

Effects on laboratory tests

Dexamethasone suppression tests may be affected by drugs which enhance the metabolic clearance of corticosteroids (see section 4.5).

False negative results in the dexamethasone suppression test have been reported in patients being treated with indomethacin or high doses of benzodiazepines or cyproheptadine.

Corticosteroids have been reported to alter the response to anticoagulant agents (see section 4.5). The prothrombin time should be checked frequently in patients receiving these combinations.

Corticosteroids may affect a wide range of diagnostic tests. They may affect brain and skeletal imaging using ^{99}Tc , by decreasing uptake of ^{99}Tc into cerebral tumours or bone respectively, and may decrease ^{123}I and ^{131}I uptake into the thyroid. Corticosteroids may alter the results of the gonadorelin test for hypothalamic-pituitary-gonadal axis function, affect thyroid function test results, and suppress skin test reactions including tuberculin and histoplasmin skin tests, and patch tests for allergy. Corticosteroids may also affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

4.5 Interaction with other medicines and other forms of interaction

Medicines that induce hepatic enzyme cytochrome P-450 isozyme 3A4 such as barbiturates, phenylbutazone, phenytoin or rifampicin, rifabutin, carbamazepine, primidone and aminoglutethimide may increase the metabolism and thus reduce the effects of corticosteroids. Ephedrine and aminoglutethimide may also increase dexamethasone metabolism.

Medicines that inhibit hepatic enzyme cytochrome P-450 isozyme 3A4 such as ketoconazole, ciclosporin or ritonavir antithyroid agents, oestrogens and other oral contraceptives may decrease hepatic metabolism and thus increase the effects of corticosteroids. The dose of corticosteroid may need to be adjusted if oestrogen therapy is commenced or stopped.

The effects of anticoagulant agents are usually decreased (but may be increased in some patients) if corticosteroids are administered concurrently. Close monitoring of the INR or prothrombin time is recommended.

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

Seizures have reportedly occurred in adult and paediatric patients receiving high dose corticosteroid therapy concurrently with cyclosporin.

Concurrent administration of dexamethasone with anticoagulants, heparin, streptokinase, urokinase, alcohol or non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin may increase the risk of gastrointestinal ulceration or haemorrhage. Aspirin should be used cautiously in conjunction with corticosteroids in patients with hypothrombinaemia. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Patients should be observed closely for adverse effects of either medicine.

Potassium loss may occur as a result of dexamethasone administration (see section 4.8). Concurrent administration of corticosteroids with potassium depleting diuretics (such as thiazides, frusemide or ethacrynic acid), carbonic anhydrase inhibitors such as acetazolamide or amphotericin B may result in severe hypokalaemia. The activity of digitalis glycosides and nondepolarising neuromuscular blocking agents may be potentiated as a result of glucocorticoid induced hypokalaemia. The efficacy of potassium supplements and potassium sparing diuretics on serum potassium concentrations may be reduced by concurrent corticosteroid administration. Monitoring of serum potassium concentration is therefore recommended.

Glucocorticoids may increase blood glucose concentrations. Dosage adjustment of asparaginase and of anti-diabetic agents such as sulphonylureas and insulins may be necessary.

The growth promoting effect of somatropin may be inhibited.

There is an increased risk of hypokalaemia if high doses of corticosteroids are given with high doses of salbutamol, salmeterol, terbutaline or formoterol.

Concurrent use of antacids may decrease absorption of corticosteroids – efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of corticosteroids.

4.6 Fertility, pregnancy and lactation

Fertility

Corticosteroids may increase or decrease the motility and number of spermatozoa in some patients.

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.

Lactation

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production or cause other unwanted effects in breastfed infants. Women taking corticosteroids should be advised not to breastfeed.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

The following adverse effects have been reported with dexamethasone therapy. Except for allergic reactions, the adverse effects listed have been associated with prolonged therapy and/or high doses.

Endocrine disorders: Adrenal suppression, menstrual irregularities, amenorrhoea, development of Cushingoid state, weight gain, secondary adrenocortical and pituitary unresponsiveness particularly in times of stress (e.g. trauma, surgery or illness), decreased carbohydrate tolerance, increased requirements for insulin or oral hypoglycaemic agents in diabetes, development of diabetes mellitus, hyperglycaemia, hirsutism, growth suppression in infancy, childhood and adolescence, increased appetite.

Cardiovascular disorders: Thromboembolism, hypertension, polymorphonuclear leucocytosis, neuropathy, vasculitis, impaired myocardial contractility (prolonged treatment), congestive heart failure in susceptible patients, myocardial rupture following recent cardiac infarction, hypertrophic cardiomyopathy in low birth weight and prematurely born infants.

Musculoskeletal and connective tissue disorders: Proximal myopathy, osteoporosis, arthropathy, muscular atrophy, muscle weakness, steroid myopathy, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones, avascular osteonecrosis, tendon rupture, myalgia. These may occur as a result of protein catabolism associated with prolonged glucocorticoid therapy.

Eye disorders: Increased intraocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, cataracts, exophthalmos, corneal or scleral thinning, retinopathy of prematurity, enhanced establishment of secondary fungal and viral eye infections.

Skin and subcutaneous tissue disorders: Impaired wound healing, hirsutism, skin atrophy, allergic dermatitis, urticaria, erythema, thin fragile skin, telangiectasia, petechiae and ecchymoses, increased sweating, may suppress skin test reactions, burning or tingling especially in the perineal area (after intravenous injection), angioneurotic oedema, acne, striae, easy bruising.

Immune system disorders: Increased susceptibility to and severity of infections with suppression of clinical symptoms and signs. Opportunistic infections, recurrence of dormant tuberculosis.

Gastrointestinal disorders: Dyspepsia, nausea, peptic ulcer with possible perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, acute pancreatitis, perforation of the small or large bowel particularly

in patients with inflammatory bowel disease, abdominal distension, ulcerative oesophagitis, oesophageal candidiasis, nausea.

Neurological disorders: Euphoric side effects, mental disturbances, psychological dependence, depression, insomnia, dizziness, headache, convulsions, increased intracranial pressure with papilloedema in children, usually after treatment withdrawal, vertigo. Aggravation of schizophrenia, aggravation of epilepsy suicidal ideation, mania, delusions, hallucinations, irritability anxiety, insomnia and cognitive dysfunction. In adults the frequency of severe psychiatric reactions has been estimated to be 5-6%.

Fluid and electrolyte disturbances: Electrolyte imbalance (retention of sodium and water with oedema and hypertension), potassium loss, hypokalaemic alkalosis, hypocalcaemia.

Metabolism and nutrition disorders: Nitrogen depletion, negative nitrogen and calcium balance due to protein catabolism.

Other effects: Allergic reactions, leucocytosis, anaphylactic or hypersensitivity reactions, weight gain, increased appetite, fatigue, malaise, hiccups.

Glucocorticoids, especially in large doses, increase susceptibility to infection, and may mask the symptoms of infection (see section 4.4).

Too rapid a reduction of corticosteroids following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A steroid withdrawal syndrome, seemingly unrelated to adrenocortical insufficiency, and consisting of anorexia, nausea and vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss and/or hypotension, has been reported following abrupt withdrawal of glucocorticoids.

Hyperpigmentation or hypopigmentation, subcutaneous and cutaneous atrophy, sterile abscess, post-injection flare (following intra-articular use) and Charcot-like arthropathy have also been associated with parenteral corticosteroid therapy.

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

Mechanism of action

Dexamethasone is a synthetic adrenocorticosteroid with glucocorticoid activity. It is one of the most active glucocorticoids, being about 25 to 30 times as potent as hydrocortisone. Unlike hydrocortisone, dexamethasone has little if any mineralocorticoid activity.

Dexamethasone has anti-inflammatory and immunosuppressant activity. 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.

The principal metabolic actions of dexamethasone are on gluconeogenesis, glycogen deposition and protein and calcium metabolism. Dexamethasone also influences the mobilisation, oxidation, synthesis and storage of fats.

Dexamethasone suppresses the release of adrenocorticotrophic hormone (ACTH) from the pituitary, resulting in inhibition of endogenous corticotrophin secretion.

Except for its use in the treatment of adrenal insufficiency, dexamethasone does not cure disease. Rather, the anti-inflammatory and immunosuppressant actions of dexamethasone suppress the symptoms associated with the disease.

5.2 Pharmacokinetic properties

Absorption

Dexamethasone phosphate (as sodium) is absorbed rapidly following intramuscular or intravenous injection. Intramuscular injections of dexamethasone phosphate give maximum plasma concentrations of dexamethasone at 1 hour. The biological half-life of dexamethasone is about 190 minutes.

Distribution

In the circulation, small amounts of dexamethasone are bound to plasma proteins.

Biotransformation

Synthetic corticosteroids such as dexamethasone are less extensively protein bound and more slowly metabolised than hydrocortisone. Dexamethasone penetrates into tissue fluids and cerebrospinal fluids. Metabolism occurs in most tissues, but primarily in the liver.

Elimination

The inactive metabolites are excreted in the urine, mainly as glucuronides and sulphates, but also as unconjugated metabolites. Small amounts of unchanged drug are also excreted in the urine. Up to 65% of a dose of dexamethasone is excreted in the urine within 24 hours.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

Reproductive and developmental toxicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ampoule

Creatinine
Hydrochloric acid
Sodium citrate dihydrate
Sodium hydroxide
Water for injection

Vial

Disodium edetate
Hydrochloric acid
Sodium citrate
Sodium hydroxide
Sodium sulfite
Water for injection

6.2 Incompatibilities

No data available.

6.3 Shelf life

Ampoule (glass)

18 months

Vial (glass)

24 months

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

DBL Dexamethasone Sodium Phosphate Injection is available in the following strengths:

Ampoule (glass)

Strength: 4 mg dexamethasone phosphate/1 mL

Pack size: 5 and 50 dose units

Vial (glass)

Strength: 8 mg dexamethasone phosphate/2 mL

Pack size: 5 and 10 dose units

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MEDICINE SCHEDULE

Prescription

8. SPONSOR

Pfizer New Zealand Limited

P O Box 3998

Auckland, New Zealand

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

Ampoule: 20 September 1984

Vial: 8 December 2011

10. DATE OF REVISION OF THE TEXT

18 December 2020

Summary table of changes

Section changed	Summary of new information
2, 3, 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 6, 6.1	Formatting and minor editorial changes to correct typographical errors
4.4	<ul style="list-style-type: none">• Addition of precautionary information for hypertrophic cardiomyopathy in prematurely born infants.• Deletion of duplicated information.
4.8	Due to the safety update in section 4.4, inclusion of “prematurely born infants” to the existing hypertrophic cardiomyopathy text for consistency.
9	<ul style="list-style-type: none">• Addition of Date of First Approval for ampoule formulation.• Revision of Date of First Approval from “8 November 2011” to “8 December 2011” for vial formulation in-line with the registered information