Dexamed Injection 8mg/2ml

Dexamethasone Phosphate

PACKAGE INSERT

PRODUCT SUMMARY

1. **TRADE NAME OF THE MEDICINAL PRODUCT**
   "Dexamed" injection
2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**
   Injection, each millilitre of aqueous solution contains Dexamethasone Sodium Phosphate 4.4mg equivalent to Dexamethasone Phosphate 4mg.
3. **PHARMACEUTICAL FORM**
   Injection for intravenous, intramuscular, intra-articular or intra-bursal administration

CLINICAL PARTICULARS

4.1 Therapeutic Indications

Injection is indicated for use in all forms of general and local glucocorticoid injection therapy and in acute cases where intravenous glucocorticoid therapy may be life-saving. For systemic administration by intravenous or intramuscular injection:

Endocrine disorders: Primary or secondary adrenocortical insufficiency (first choice is hydrocortisone or cortisone, but synthetic analogues may be used with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is particularly important), congenital adrenal hyperplasia.

Non-endocrine disorders: Use in non-endocrine corticosteroid responsive conditions, including:

Allergy and anaphylaxis: angioneurotic oedema and anaphylaxis.

Gastro-intestinal: Crohn's disease, ulcerative colitis.

Infection (with appropriate chemotherapy): military tuberculosis and endotoxic shock.

Neurological disorders: raised intra-cranial pressure secondary to cerebral tumours and infantile spasms.

Respiratory: bronchial asthma and aspiration pneumonitis.

Skin disorders: toxic epidermal necrolysis.

Shock: adjunctive treatment where high pharmacological doses are needed. Treatment is an adjunct, not a substitute, for specific and supportive measures. Dexamethasone has been demonstrated to be beneficial in early treatment of shock, although it may not influence overall survival.

Local administration: it is suitable for intra-articular or soft tissue administration, short term, as adjunctive therapy in:

Soft tissue disorders: carpal tunnel syndrome, tenosynovitis.

Intra-articular disorders: rheumatoid arthritis and osteoarthritis with an inflammatory component.

It may be injected intralesionally in skin disorders such as cystic acne vulgaris, localised lichen simplex and keloids.

4.2 Posology and Method of Administration

NOTE: doses are expressed as mg dexamethasone phosphate for the injection. Dexamethasone phosphate 4mg is equivalent to approximately 3.33mg dexamethasone.

Glucocorticoid dosage generally depends on the patient response and the severity of the condition. In certain circumstances, such as a change in the clinical prognosis, or in stress, extra dosage adjustments may be needed. Glucocorticoid therapy should be discontinued if there is no favourable response following two days of therapy.

Adults: Dosage must be individualised to the patient and to the disease. The lowest possible dosage to control the disease must be used to minimise side effects. Usual parenteral dose range is one third to half the oral dose, given every twelve hours. Usual initial dose is 0.5mg to 20mg (0.125ml–5ml) a day. Initial dosage should be maintained or adjusted until a satisfactory response is noted. When a favourable response is obtained, the effective maintenance dose should be determined by decrease of dose at suitable intervals and by small increments to obtain the lowest dose with satisfactory clinical response. Chronic dosage should not exceed the equivalent of 0.5mg dexamethasone per day (equivalent to 0.6mg dexamethasone phosphate, 0.15ml injection). If treatment is stopped following administration for more than a few days, it should be done gradually.

Shock (of surgical, traumatic or haemorrhagic origin): usually 2mg–6mg/kg bodyweight as a single intravenous injection. It can be repeated in two to six hours if shock persists. High doses should only be administered until the patient's condition has stabilised, usually no longer than 48–72 hours.

Cerebral oedema: associated with primary/metastatic brain tumour, pre-operative preparation of patients with increased intracanial pressure secondary to brain tumour, 10mg intravenously followed by 4mg intramuscularly every six hours until subsidence of symptoms. Response is usually obtained in 12–24 hours, thereafter dosage may be reduced after 2 – 4 days and gradually discontinued after 5 – 7 days. High doses of the injection are recommended for initiation of short term intensive therapy in life threatening cerebral oedema. Doses are subsequently scaled down, eventually reducing to zero, over a seven to ten day period, see table. When maintenance therapy is required, tablets should be substituted as soon as possible.

Suggested high dose therapy in cerebral oedema	
Adults:	
Initial dose	50mg intravenous
1st day	8mg intravenous every 2 hours
2nd day	8mg intravenous every 2 hours
3rd day	8mg intravenous every 2 hours
4th day	8mg intravenous every 2 hours
5th to 8th days	8mg intravenous every 4 hours
Thereafter	decrease by daily reduction of 4mg
Children (Body weight 35kg and greater)	
Initial dose	25mg intravenous
1st day	4mg intravenous every 2 hours
2nd day	4mg intravenous every 2 hours
3rd day	4mg intravenous every 2 hours
4th day	4mg intravenous every 4 hours
5th to 8th days	4mg intravenous every 6 hours
Thereafter	decrease by daily reduction of 2mg
Children (Body weight less than 35kg)	
Initial dose	20mg intravenous
1st day	4mg intravenous every 3 hours
2nd day	4mg intravenous every 3 hours
3rd day	4mg intravenous every 3 hours
4th day	4mg intravenous every 6 hours
5th to 8th days	4mg intravenous every 6 hours
Thereafter	decrease by daily reduction of 1mg

Intrasynovial/intralesional/soft tissue injection: Use only when one or two joints affected. Suggested doses are in the table below:

Site of injection	*Dexamethasone phosphate*
Large joint	2mg – 4mg (0.5ml – 1ml)
Small joint	0.8mg – 1mg (0.2ml – 0.25ml)
Bursae	2mg – 3mg (0.5ml – 0.75ml)
Tendon sheath	0.4mg – 1mg (0.1ml – 0.25ml)
Infiltration of soft tissue	2mg – 6mg (0.5ml–1.5ml)
Ganglia	1mg – 2mg (0.25ml–0.5ml)

Injections should be done once every three to five days to once every two to three weeks, dependent upon the response of the patient.

Children: Use should be limited to a single dose on alternate days in order to minimise suppression of hypothalamo-pituitary-adrenal axis.

Elderly: Treatment, particularly if long term, must be planned being aware of the more serious consequences of the common side effects in old age. Of especial concern are osteoporosis, diabetes, hypokalaemia, hypertension, susceptibility to infection and skin thinning. Very close clinical supervision is required.

4.3 Contra-indications

Hypersensitivity to any ingredient.

Systemic infection, unless specific anti-infective therapy also used.

In bacteraemia, systemic fungal infection, unstable joints, infection at injection site (i.e. septic arthritis resulting from gonorrhoea or tuberculosis) local injection is contraindicated. Where use of glucocorticoids may be lifesaving, contraindications do not usually apply.

4.4. Special Warnings and Precautions for Use

Undesirable effects can be minimised by use of the lowest effective dose for minimum period, and by administration of daily dose single morning dose, or, if possible, as a morning dose on alternate days. It is necessary to frequently review patients to titrate the dose against disease activity.

During prolonged therapy, adrenal cortical atrophy develops. This may persist for years after therapy cessation. Withdrawal of corticosteroids in prolonged therapy must always be gradual to prevent acute adrenal insufficiency. Dosage should be tapered off over weeks or months, depending upon dose and duration of therapy. In prolonged therapy, any inter-current illness, surgical procedure or trauma will require a temporary increase in dosage. If prolonged therapy has stopped, temporary reintroduction of corticosteroids may be necessary.

It is recommended that patients carry a "Steroid Treatment Card". This should give clear guidance on precautions to minimise risk and provide full details on the prescriber, drug, dose and treatment duration. The inflammatory response and immune function are suppressed increasing susceptibility to, and severity of infection. The clinical, presentation of infection may be atypical, and serious infections (i.e. tuberculosis, septicaemia) can be masked and reach an advanced stage before being diagnosed. Appropriate anti-microbial therapy should accompany glucocorticoid therapy when necessary.

Of particular concern is chickenpox, as this usually minor illness may be fatal in immunosuppressed patients. Patients or parents of children without a definite history of chickenpox must be advised to avoid close personal contact with chickenpox or herpes zoster. If exposure occurs, urgent medical attention must be sought. Exposed non-immune patients on systemic corticosteroids, or who have used them in the preceding three months, need passive immunisation with varicella zoster immunoglobulin, this should be administered within ten days of exposure. In the case of a confirmed diagnosis of chickenpox, this needs specialist care and urgent medical treatment. Corticosteroids should not be stopped and an increase in dose may be necessary. Individuals with impaired immune response should not be given live vaccines, and the antibody response to other vaccines may be reduced.

In patients with the following conditions, particular care is needed when considering the use of systemic corticosteroids, and frequent patient monitoring is necessary:

- Osteoporosis, not that post-menopausal women are particularly at riski	- Hypertension or congestive heart failure
- Existing, or previous history of, severe affective disorders, especially steroid psychosis	- Diabetes mellitus, or a family history of diabetes
- Glaucoma, or a family history of glaucoma	- Liver failure
- Renal insufficiency	- Epilepsy
- Peptic ulceration	- Migraine
- Parasitic infestation, especially amoebiasis	- Incomplete natural growth as prolonged administration of glucocorticoids may speed up epiphyseal closure
- Cushing's syndrome patients	

In children, corticosteroids cause dose related growth retardation in infancy, childhood and adolescence. This may be irreversible. Growth and development of infants/children on long term corticosteroid therapy must be carefully monitored.

In the elderly, common adverse effects of systemic corticosteroid therapy may be associated with more severe consequences, especially in respect to osteoporosis, hypokalaemia, hypertension, diabetes, skin thinning and infection susceptibility. Close clinical supervision and observation is essential in this group of patients.

In local treatment by injection of conditions such as tendinitis or teno-synovitis, care must be taken to inject into the space between the tendon and the tendon sheath as cases of ruptured tendon have been reported. Especially in patients with a history of allergy, serious anaphylactoid reactions have occurred following glucocorticoid administration.

These have included glottis oedema, bronchospasm and urticaria.

If anaphylactoid reaction occurs, it is recommended to use immediate slow intravenous injection of 0.1ml - 0.5ml adrenaline solution 1: 1000 (0.1mg–0.5mg adrenaline dependent upon body weight), aminophylline intravenous, and artificial respiration if required.

4.5. Interactions with other Medicaments and other forms of Interaction

The metabolism of corticosteroids is enhanced by aminoglutethimide, carbamazepine, ephedrine, phenobarbitone, phenylbutazone, phenytoin, primidone, rifabutin and rifampicin, thus its therapeutic effect may be reduced. Corticosteroids antagonise the desired effects of anti- hypertensives, diuretics and hypoglycaemic agents (including insulin).

The hypokalaemic effects of acetazolamide, carbenoxolone, loop diuretics and thiazide diuretics are enhanced by corticosteroids. Concurrent corticosteroid therapy may enhance the efficacy of coumarin anticoagulants, close monitoring of INR or prothrombin time is necessary to avoid spontaneous bleeding.

Corticosteroids increase salicylate renal clearance, salicylate intoxication may result from steroid withdrawal. Close monitoring of patients on non-steroidal anti-inflammatory drugs is advised as the incidence and/or severity of gastro-intestinal ulceration may increase.

4.6. Pregnancy and Lactation

The use of dexamethasone in pregnancy, nursing mothers, or women of childbearing potential requires that possible benefits of the drug be weighed against the potential hazards, to the mother and embryo or fetus.

4.7. Effects on Ability to Drive and Use Machines

No reported effects.

4.8. Undesirable Effects

The frequency of predictable undesirable effects, including suppression of hypothalamic-pituitary-adrenal system, correlates with dosage, drug potency, timing of dose and treatment duration (see also "Special Warnings and Precautions for Use").

With the injection only, local adverse reactions include post injection flare, painless destruction of the joint (similar to Charcots arthropathy) especially with repeated intra-articular administration. Local injections may produce systemic effects.

Endocrine/metabolic: hypothalamic-pituitary-adrenal axis suppression, suppression of growth (infancy/childhood/adolescence), irregular menstruation and amenorrhoea. Cushingoid faces, hirsutism, premature epiphyseal closure, weight gain, carbohydrate tolerance impairment and increased anti-diabetic therapy requirement. Increased appetite. Negative calcium and protein balance.

Anti-inflammatory and immunosuppresive: severity and susceptibility to infection increased with suppression of clinical symptoms, recurrence of dormant tuberculosis and opportunistic infections.

Decrease in response to vaccination and skin tests (see also "Special Precautions and Warnings for Use").

Musculoskeletal: osteoporosis, fractures of long bones and vertebra, avascular osteonecrosis, tendon rupture and proximal myopathy.

Electrolyte and Fluid disturbance: sodium retention, water retention, hypertension, hypokalaemic alkalosis and potassium loss.

Neuropsychiatric: aggravation of schizophrenia, depression, insomnia and psychological dependence. In children, usually after treatment withdrawal, increased intra-cranial pressure with papilloedema

(pseudotumour cerebri). Epilepsy aggravation. Psychic disturbance which can range from euphoria to frank psychotic manifestations.

Opthalmic: intra-ocular pressure elevation, glaucoma, papilloedema, corneal or scleral thinning, posterior subcapsular cataracts, worsening of opthalmic viral or fungal infection.
Gastrointestinal: dyspepsia, peptic ulceration (with perforation and haemorrhage), acute pancreatitis, candidiasis, abdominal distension and vomiting.
Dermatological: acne, bruising, impaired healing, skin atrophy, striae, telangiectasia.
General: hypersensitivity - including anaphylaxis, leucocytosis and thromboembolism.
Withdrawal symptoms/signs: following prolonged treatment, too rapid dosage reduction of corticosteroid can cause acute adrenal insufficiency, hypotension and death. A withdrawal syndrome may occur, including arthralgia, conjunctivitis, fever, myalgia, painful and itchy skin nodules, rhinitis and weight loss.

4.9. Overdose
Definition of overdose is difficult as therapeutic dose varies widely according to indication and patient response. In overdose it would be anticipated that corticosteroid adverse effects would be severe and greater. Symptomatic and supportive treatment is recommended.

PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic Properties
Dexamethasone is a synthetic glucocorticoid with an anti-inflammatory potency about seven fold that of prednisolone. As with other glucocorticoids, dexamethasone also possesses anti-allergic, antipyretic and immunosuppressive properties. It acts on the HPA at specific receptors on the plasma membrane. It diffuses across cell membranes in other tissues and following complexation with specific cytoplasmic receptors, enters the cell nucleus and stimulates protein synthesis.
It has practically no water and salt retaining properties, making it useful in patients with cardiac failure or hypertension. The long biological half-life (36h – 54h) makes it suitable for use in conditions where continuous glucocorticoid action is wanted.

5.2. Pharmacokinetic Properties
Generally corticosteroids are well absorbed from the gastro-intestinal tract. Following administration of dexamethasone sodium phosphate, it 190 minutes in adults. Intravenous administration gives a rapid onset of action of comparatively short duration. Intramuscular administration results in a slower onset of action with a comparatively longer duration. For this reason the intravenous route is the route of choice in initial dosage in life threatening situations, with maintenance being more appropriate by intramuscular administration.
Corticosteroids are rapidly distributed to all body tissues, they cross the placenta and are excreted in small quantities in breast milk. In the circulation it is extensively bound to plasma proteins, the majority to
globulin (high affinity, low capacity) and less so to albumin (low affinity, high capacity). The plasma binding is proportionate to the dose, and in very high doses the majority is unbound. In hypoalbuminaemia the proportion of unbound dexamethasone increases.
Metabolism is mainly in the liver, but also in the kidney, excretion is mainly in urine as unconjugated steroids. Impaired renal function does not significantly influence the elimination of dexamethasone, whereas impaired hepatic function will prolong the elimination half-life in severe impairment.

5.3. Preclinical Safety Data
Not applicable.

PHARMACEUTICAL PARTICULARS
6.1. List of Excipients
Sodium citrate, disodium edetate, creatinine and water for injections, sodium hydroxide, hydrochloric acid

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

6.4. Special Precautions for Storage
Store below 30°C in the original package, in order to protect from light. Do not refrigerate or freeze. For the reconstituted product, chemical and physical in-use stability was demonstrated for 24hours when diluted with isotonic saline solution, Ringer's solution, Glucose solution 5%, Glucose solution 10% and Dextrose solution 5% at 25°C ± 2°C, 60% ± 5% RH or 2–8°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8 °C , unless dilution has taken place in controlled and validated aseptic conditions.

6.5. Nature and Contents of Container
Injection: Clear glass ampoules containing two (2) millilitres of solution in a carton containing 10 or 100 ampoules.

6.6. Instruction for Use/Handling
Dexamed Injection 8mg/2ml is preferably administered by direct intravenous injection or injected into the infusion tube. Solution for injection is compatible with the following infusion solutions and intended to be used within 24 hours:
- Isotonic saline solution
- Ringer's solution
- Glucose solution 5%
- Glucose solution 10%
- Dextrose solution 5%

When used in combination with solutions for infusion, each supplier's information on their solutions for infusion, including information on compatibility, contraindications, undesirable effects and interactions should be considered.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

ADMINISTRATIVE DATA
Name and address of the Manufacturer
Medochemie Ltd (Ampoule Injectable Facility) Agios Athanassios Industrial Area, Iapetou 48, Limassol, 4101, Cyprus

Product Registration Holder
Komedic Sdn Bhd, 4 Jalan PJS 11/14, Bandar Sunway, 46150 Petaling Jaya, Selangor - Malaysia

Date of (Partial) Revision of the Text: July 2025