Dexamethasone 2mg Tablets

Summary of Product Characteristics Updated 16-Nov-2015 | Auden Mckenzie (Pharma Division) Ltd (a subsidiary of Actavis PLC)

1. Name of the medicinal product
Dexamethasone 2mg Tablets

2. Qualitative and quantitative composition
Each tablet contains 2.0 mg dexamethasone.
Contains lactose monohydrate (68.8mg per tablet); for a full list of excipients, see section 6.1.

3. Pharmaceutical form
Round white tablet, one side marked DX

4. Clinical particulars

4.1 Therapeutic indications
Indicated in a wide variety of disorders amenable to glucocorticoid therapy, as well as an adjunct in the control of cerebral oedema.

4.2 Posology and method of administration
In general, glucocorticoid dosage depends on the severity of the condition and response of the patient. Under certain circumstances, for instance in stress and changed clinical picture, extra dosage adjustments may be necessary. If no favourable response is noted within a couple of days, glucocorticoid therapy should be discontinued.

1. Adults
Usually, daily oral dosages of 0.5 - 10 mg are sufficient. In some patients higher dosages may be temporarily required to control the disease. Once the disease is under control, the dosage should be reduced or tapered off to the lowest suitable level under continuous monitoring and observation of the patient. (See Section 4.4)

For a short dexamethasone suppression test, 1mg dexamethasone is given at 11 pm and plasma cortisol measured the next morning. Patients who do not show a decrease in cortisol can be exposed to a longer test: 500 micrograms dexamethasone is given at 6 hourly intervals for 48 hours followed by 2mg every 6 hours for a further 48 hours. Twenty-four hour urine collections are made before, during and at the end of the test for determination of 17-hydroxycorticosteroids.

2. Children
0.01-0.1mg/kg of body weight daily
Dosage of glucocorticoids should be adjusted on the basis of the individual patient's response.

4.3 Contraindications
• Systemic infection unless specific antimicrobial therapy given.
• Avoid live virus vaccines in those receiving immunosuppressive doses as the serum antibody response is diminished.
• Hypersensitivity to dexamethasone or to any of the ingredients.
In general, no contraindications apply in conditions where use of glucocorticoids may be life saving.

4.4 Special warnings and precautions for use
Every patient should receive the patient information leaflet. Patients on long-term dexamethasone treatment should carry a Steroid Treatment Card which gives guidance on minimising risk and provides details of prescriber, drug, dosage and duration of treatment. Patients/and or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 pharmacokinetic interactions that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.
Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

**Adrenal Suppression** Abrupt withdrawal after prolonged therapy with corticosteroids may lead to acute adrenal insufficiency, hypotension or death. During prolonged therapy with corticosteroids, adrenal atrophy develops and may persist for years after stopping. Withdrawal may also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss. To compensate for a diminished adrenocortical response caused by prolonged corticosteroid treatment, any significant intercurrent illness, trauma, or surgical procedure requires a temporary increase in corticosteroid dose, or if already stopped, a temporary re-introduction of corticosteroid treatment. Anaesthetists must therefore know whether a patient is taking or has been taking a corticosteroid, to avoid a precipitous fall in blood pressure during anaesthesia or in the immediate postoperative period. A suitable regimen for corticosteroid replacement, in patients who have taken more than 1.5 mg dexamethasone daily within 3 months of surgery, is:

**Minor surgery under general anaesthesia**—usual oral corticosteroid dose on the morning of surgery or hydrocortisone 25–50 mg (usually the sodium succinate) intravenously at induction; the usual oral corticosteroid dose is recommenced after surgery

**Moderate or major surgery**—usual oral corticosteroid dose on the morning of surgery and hydrocortisone 25–50 mg intravenously at induction, followed by hydrocortisone 25–50 mg 3 times a day by intravenous injection for 24 hours after moderate surgery or for 48–72 hours after major surgery; the usual pre-operative oral corticosteroid dose is recommenced on stopping hydrocortisone injections.

**Infections** Prolonged courses of dexamethasone increase susceptibility to infections and severity of infections; clinical presentation of infections may also be atypical. Serious infections e.g. septicaemia and tuberculosis may reach an advanced stage before being recognised, and amoebiasis or strongyloidiasis may be activated or exacerbated (exclude before initiating dexamethasone in those at risk or with suggestive symptoms). Fungal or viral ocular infections may also be exacerbated. Appropriate anti-microbial therapy should accompany glucocorticoid therapy when necessary e.g. in tuberculosis and viral and fungal infections of the eye. **CHICKENPOX** 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 personal contact with chickenpox or herpes zoster and if exposed, they should seek urgent medical attention. Unless they have had chickenpox, patients receiving oral dexamethasone for purposes other than replacement should be regarded as being at risk of severe chickenpox. Manifestations of fulminant illness include pneumonia, hepatitis and disseminated intravascular coagulation; rash is not necessarily a prominent feature. Passive immunisation with varicella–zoster immunoglobulin is needed for exposed non-immune patients currently taking dexamethasone tablets or for those who have used them within the previous 3 months; varicella–zoster immunoglobulin should preferably be given within 3 days of exposure and no later than 10 days. **MEASLES** Patients taking dexamethasone 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.

**Infants, Children and adolescents** Growth retardation - possibly irreversible.

**Elderly** Close supervision required particularly on long-term treatment. The common adverse events 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.

**Preterm neonates:** Available evidence suggests long-term neurodevelopmental adverse events after early treatment (< 96 hours) of premature infants with chronic lung disease at starting doses of 0.25mg/kg twice daily.

Close supervision is required to avoid life-threatening reaction. Frequent monitoring is required in the following situations:

- history of tuberculosis (or X-ray changes)
- hypertension
- recent myocardial infarction (rupture reported)
- congestive heart failure
- renal impairment
- diabetes mellitus including family history
- osteoporosis (post-menopausal women at special risk)
- glaucoma (including family history)
- corneal perforation
- severe affective disorders (particularly if history of steroid-induced psychosis)
- epilepsy

Withdrawal of dexamethasone Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids must therefore always be gradual to avoid adrenal insufficiency, being tapered off over weeks or months according to the dose and duration of treatment. In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg of dexamethasone) 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 the 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 of 1 mg dexamethasone is reached, dose reduction should be slower to allow the HPA axis to recover. The Committee on Safety of Medicines has recommended that gradual withdrawal of systemic corticosteroids should be considered in those whose disease is unlikely to relapse and have

- recently received repeated courses (particularly if taken for longer than 3 weeks)
- taken a short course within 1 year of stopping long-term therapy
- other possible causes of adrenal suppression
- received more than 6 mg dexamethasone daily
- been given repeat doses in the evening
- received more than 3 weeks’ treatment

Systemic corticosteroids may be stopped abruptly in those whose disease is unlikely to relapse and who have received treatment for 3 weeks or less and who are not included in the patient groups described above. During corticosteroid withdrawal the dose may be reduced rapidly down to physiological-equivalent doses – approximately 1 mg dexamethasone daily and then reduced more slowly. Assessment of the disease may be needed during withdrawal to ensure that relapse does not occur.

Patients with rare heredity problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Dexamethasone may interact with other products as follows:-

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<tr>
<th>Product</th>
<th>Effect</th>
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<tr>
<td>Aprepitant</td>
<td>metabolism of dexamethasone inhibited therefore reduce dose of dexamethasone</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>dexamethasone possibly reduces plasma concentration of caspofungin; consider increasing dose of caspofungin</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>metabolism of dexamethasone accelerated</td>
</tr>
<tr>
<td>Indinavir Lopinavir Saquinavir</td>
<td>dexamethasone possibly reduces plasma concentration</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>plasma concentration of dexamethasone possibly increased</td>
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As dexamethasone is a Corticosteroid, the following interactions could occur:

<table>
<thead>
<tr>
<th>Product</th>
<th>Effect</th>
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<tbody>
<tr>
<td>ACE Inhibitors Adrenergic neurone blockers Alpha-blockers</td>
<td>antagonism of hypotensive effect</td>
</tr>
<tr>
<td>Angiotensin-II Receptor Agonists Beta-blockers Calcium-channel blockers (Dihydropyridine calcium-channel blockers include amlodipine, felodipine, isradipine, lacidipine, lercanidipine, nicardipine, nifedipine, nimodipine, and nisoldipine) Clonidine Diazoxide Hydralazine Methyldopa Minoxidil Moxonidine Nitrates Nitroprusside</td>
<td>increased risk of hypokalaemia</td>
</tr>
<tr>
<td>Acetazolamide Amphoterin® Carbenoxolone Cardiac Glycosides Diuretics, Loop Diuretics, Thiazide and Related Theophylline</td>
<td>increased risk of hypokalaemia</td>
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β-Sympathomimetics (high dose) monitor plasma K in severe asthma

Aminoglutethimide Barbiturates* metabolism of corticosteroids accelerated (reduced effect)

Carbamazepine* Phenytoin* Primidone* Rifamycins*

Amphotericin* avoid concomitant use unless amphotericin needed to control reactions; close monitoring required – amphotericin nephrotoxic

Antidiabetics antagonism of hypoglycaemic effect

Aspirin NSAIDs increased risk of gastro-intestinal bleeding and ulceration

Aspirin corticosteroids reduce plasma concentration of salicylate

Coumarins* corticosteroids may enhance or reduce anticoagulant effect of coumarins (high-dose corticosteroids enhance anticoagulant effect)

Diuretics antagonism of diuretic effect

Erythromycin Ketoconazole metabolism of corticosteroids possibly inhibited

Methotrexate* increased risk of haematological toxicity

Mifepristone effect of corticosteroids may be reduced for 3–4 days after mifepristone

Nephrotoxic/Cytotoxic drugs close monitoring required

Oestrogens plasma concentration of corticosteroids increased by oral contraceptives containing oestrogens; low dose in HRT unlikely to induce interactions

Somatropin growth-promoting effect of somatropin may be inhibited

Vaccines* high doses of corticosteroids impair immune response to vaccines; avoid concomitant use with live vaccines. Live vaccines should be postponed until at least 3 months after stopping corticosteroids

Calcium salts Corticosteroids reduce absorption of calcium salts

Sodium phenylbutyrate Corticosteroids possibly reduce effects of sodium phenylbutyrate

*Potentially hazardous interaction

4.6 Fertility, pregnancy and lactation

Dexamethasone readily crosses the placenta with minimal inactivation but there is no convincing evidence that systemic corticosteroids increase the incidence of congenital abnormalities such as cleft palate or lip.

Prolonged or repeated administration during pregnancy increases the risk of uterine growth retardation.

Any adrenal suppression in the neonate following prenatal exposure usually resolves spontaneously and is rarely clinically important.

Systemic effects in the infant are unlikely with a maternal dose of dexamethasone up to 6 mg daily (= 40 mg prednisolone); the infant's adrenal function should be monitored with higher doses.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intrauterine 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. See also section 5.3 of the SmPC.
Corticosteroids may be excreted in small amounts in breast milk.
Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

4.7 Effects on ability to drive and use machines
Steroids may cause vertigo, vision disorders or muscle weakness. If affected patients should be advised not to drive or operate machinery.

4.8 Undesirable effects
The incidence of adverse effects rises steeply if dosage increases much above physiological values, represented by just over 1mg of dexamethasone. Short courses at high doses for emergencies appear to cause fewer side-effects than prolonged courses with lower doses. Thus, adverse effects are minimised by using the lowest effective dose and for the minimum period possible. Psychiatric disorders are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%.
Adverse glucocorticoid effects lead to mobilisation of calcium and phosphorous, with osteoporosis and spontaneous fractures, particularly in the elderly. Hyperglycaemia may precipitate or accentuate diabetes leading to an increase in the insulin requirements of diabetic patients. Suppression of clinical symptoms and signs by the anti-inflammatory, analgesic and antipyretic effects of glucocorticoids may mask an increased susceptibility to infection and increased severity of infection brought about by the immunosuppressive effects. As a number of cases of fatal or near-fatal cases of chickenpox (varicella) have been reported, passive immunisation should be given to non-immune patients receiving corticosteroids. Impaired tissue repair and immune function can lead to delayed wound healing. The negative feedback effects of glucocorticoids on the hypothalmic-pituitary-adrenal axis may lead to adrenal atrophy. This produces secondary adrenal insufficiency which may become manifest following overly rapid withdrawal of treatment or be precipitated by some stress such as infection or trauma.
There are no modern clinical studies available that can be used to determine the frequency of individual undesirable effects. Therefore, all the undesirable effects listed are classed as “frequency unknown”.

Infections and infestations:
Infection susceptibility increased (including septicaemia, tuberculosis, chickenpox, measles, fungal and viral infections).

Blood & lymphatic system disorders:
Coagulation abnormal (increase in coagulability of blood may lead to thromboembolic complications); leukocytosis

Immune system disorders:
Hypersensitivity; anaphylactic reaction.

Endocrine disorders:
Adrenal atrophy; adrenal insufficiency (symptoms include: menstrual disorders; amenorrhoea; hirsutism; weight gain; nitrogen balance negative; calcium balance negative; increased appetite); adrenal suppression (of the foetus or neonate following maternal administration); adrenal hyperactivity (Cushingoid symptoms include moon face; hirsutism; buffalo hump; flushing; bruising; ecchymoses; striae; acne); growth suppression in children; steroid withdrawal syndrome (see below).
Withdrawal should be gradual in those who have been treated for any length of time. Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4). Withdrawal may also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss.
Cushingoid symptoms are usually reversible on withdrawal of treatment, but dosage must always be tapered gradually to avoid symptoms of acute adrenal insufficiency.

Metabolism & nutrition disorders
Fluid imbalance; electrolyte disturbance.

Psychiatric disorders
Affective disorders (including irritability, euphoria, depressed mood, mood disorder, suicidal ideation); psychotic disorder (including mania, delusion, hallucination, schizophrenia aggravated); behavioural disorder; anxiety; sleep disturbances; cognitive disorders (including confusional state and amnesia); euphoria; dependence psychological; depression; insomnia; psychosis; schizophrenia aggravated; epilepsy aggravated; paranoid state; depression suicidal (particularly in patients with a history of mental disorder).

Nervous system disorders:-
Benign intracranial hypertension; headache.

Eye disorders
Intraocular pressure increased; glaucoma; papilloedema (may be associated with increased intracranial pressure in children, usually after withdrawal); cataract subcapsular; corneal thinning; scleral thinning; eye infection viral; eye infection fungal.

Ear & labyrinth disorders
Vertigo.

Cardiac disorders
Myocardial rupture (post-infarct); congestive heart failure.

Respiratory disorders
Hiccups.

Gastrointestinal disorders
Nausea; dyspepsia; abdominal distension; acute pancreatitis; oesophageal ulceration; oesophageal candidiasis; peptic ulcer; peptic ulcer perforation; peptic ulcer haemorrhage.

Skin & subcutaneous tissue disorders
Skin atrophy; bruising; telangiectasia; hyperhidrosis; petechiae; urticaria.

Musculoskeletal, connective tissue & bone disorders
Bone fracture spontaneous; tendon rupture; muscle atrophy; myopathy; avascular necrosis femoral head (at high doses).

General & administration site disorders:
Malaise ; vaccination complication (decreased responsiveness to vaccination); skin test abnormal; wound healing delayed.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme (Website: www.mhra.gov.uk/yellowcard).

4.9 Overdose
It is difficult to define an excessive dose of a corticosteroid as the therapeutic dose will vary according to indication and patient requirements.

Overdosage or prolonged use may exaggerate glucocorticoid adverse effects. Treatment should be symptomatic and supportive with the dosage of dexamethasone being reduced or slowly withdrawn where possible.

5. Pharmacological properties
5.1 Pharmacodynamic properties
[ATC Code: H02AB02 Systemic Hormonal Preparations (excluding sex hormones and insulins); Corticosteroids for Systemic Use; Plain; Glucocorticoids; Dexamethasone]
The adrenal cortex synthesises corticosteroids. Corticosteroids are traditionally divided into those with predominantly glucocorticoid actions and those of which the actions are primarily mineralocorticoid. The endogenous glucocorticoids are under regulatory control from the hypothalamus and pituitary via releasing hormones. In return, the glucocorticoids act to inhibit production and release of the releasing hormones by a negative feedback mechanism. Glucocorticoid actions are wide ranging. They have potent anti-inflammatory and immunosuppressive effects, achieved at least partly through inhibition of various cytokines. It is primarily these effects which are made use of clinically. Glucocorticoids also have profound metabolic effects on blood glucose concentration, glycogen deposition, protein breakdown, lipolysis and effects on calcium uptake and excretion. They also have effects on the function of the cardiovascular system, kidneys, skeletal muscle and the CNS.

Dexamethasone is a synthetic glucocorticoid of which the anti-inflammatory potency on a weight for weight basis is 7 times greater than that of prednisolone. Pharmacological doses of corticosteroids/glucocorticoids are used when palliative anti-inflammatory or immunosuppressant effects are required to suppress the clinical manifestations of disease in a wide range of disorders considered to have inflammatory or immunological components.
Lack of mineralocorticoid (water and salt-retaining) properties makes dexamethasone particularly suitable for treating conditions where water retention would be a disadvantage, for example, cerebral oedema. Coupled with its long duration of action, dexamethasone is also indicated for conditions such as congenital adrenal hyperplasia which require suppression of corticotrophin secretion.

5.2 Pharmacokinetic properties

Dexamethasone is readily absorbed from the gastrointestinal tract. Corticosteroids are rapidly distributed to all body tissues. They cross the placenta and may be excreted in small amounts in breast milk. Corticosteroids bind extensively to plasma proteins, though the synthetic ones are less extensively protein bound than cortisol. They also tend to have longer half-lives; the biological half-life of dexamethasone in plasma is 3-4 hours. Corticosteroids are metabolised mainly in the liver but also in other tissues and are excreted in the urine.

The slower metabolism and lower protein-binding affinity of the synthetic corticosteroids compared with the natural corticosteroids may account for their increased potency.

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

Lactose monohydrate
Microcrystalline cellulose
Sodium starch glycolate (type A)
Colloidal hydrated silica
Magnesium stearate (E470b)

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Protect from light

6.5 Nature and contents of container

PVC/Aluminium blister strips of 10 tablets in packs of 50 and 100 tablets.
Hospital pack: Polypropylene bottle of 500 tablets with polypropylene Snap-Secure cap.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder

Auden Mckenzie (Pharma Division) Ltd
Mckenzie House
Bury Street
Ruislip
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HA4 7TL
UK
8. Marketing authorisation number(s)
PL 17507/0053

9. Date of first authorisation/renewal of the authorisation
08/12/2006

10. Date of revision of the text
20/05/2015

Company Contact Details
Auden McKenzie (Pharma Division) Ltd (a subsidiary of Actavis PLC)
http://www.actavis.co.uk

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<th>Address</th>
<th>Telephone</th>
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<tbody>
<tr>
<td>Mckenzie House, Bury Street, Ruislip, Middlesex, HA4 7TL</td>
<td>+44 (0)1895 627 480</td>
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<tr>
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