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Summary of Product Characteristics last updated on the eMC: 14/06/2013

Dexsol 2mg/5ml Oral Solution

1. Name of the medicinal product

Dexsol 2mg/5ml Oral Solution

2. Qualitative and quantitative composition

Dexamethasone 2mg/5ml (as dexamethasone sodium phosphate)

Excipients:

Propylene glycol 450mg/5ml

Garden mint flavour (containing 0.61mg/5ml propylene glycol)

Liquid maltitol 1375mg/5ml

Liquid sorbitol 700mg/5ml

For a full list of excipients, see section 6.1

3. Pharmaceutical form

Oral Solution

A colourless to faint yellow solution with odour of mint.

4. Clinical particulars

4.1 Therapeutic indications

Dexamethasone is a corticosteroid. It is designed for use in certain endocrine and non-endocrine disorders, in certain cases of cerebral oedema and for diagnostic testing of adrenocortical hyperfunction.

Endocrine disorders:

Endocrine exophthalmos.

Non-endocrine disorders:

Dexamethasone may be used in the treatment of non-endocrine corticosteroid responsive conditions including:

Allergy and anaphylaxis: Anaphylaxis.

Arteritis collagenosis: Polymyalgia rheumatica, polyarteritis nodosa.

Haematological disorders: Haemolytic anaemia (also auto immune), leukaemia, myeloma, idiopathic thrombocytopenic purpura in adults, reticulolymphoproliferative disorders (see also under oncological disorders).

Gastroenterological disorders: For treatment during the critical stage in: ulcerative colitis (rectal only); regional enteritis

(Crohn's disease), certain forms of hepatitis.

Muscular disorders: Polymyositis.

Neurological disorders: Raised intra-cranial pressure secondary to cerebral tumours, acute exacerbations of multiple sclerosis.

Ocular disorders: Anterior and posterior uveitis, optic neuritis, chorioretinitis, iridocyclitis, temporal arteritis, orbital pseudotumour.

Renal disorders: Nephrotic syndrome

Pulmonary disorders: Chronic bronchial asthma, aspiration pneumonitis, chronic obstructive pulmonary disease (COPD), sarcoidosis, allergic pulmonary disease such as farmer's and pigeon breeder's lung, Löffler's syndrome, cryptogenic fibrosing alveolitis.

Rheumatic disorders: some cases or specific forms (Felty's syndrome, Sjörger's syndrome) of rheumatoid arthritis, including juvenile rheumatoid arthritis, acute rheumatism, lupus erythematosus disseminatus, temporal arteritis (polymyalgia rheumatica).

Skin disorders: Pemphigus vulgaris, bullous pemphigoid, erythrodermas, serious forms of erythema multiforme (Stevens-Johnson syndrome), mycosis fungoides, bullous dermatitis herpetiformis.

Oncological Disorders: Lymphatic leukaemia, especially acute forms, malignant lymphoma (Hodgkin's disease, non-Hodgkin's lymphoma), metastasized breast cancer, hypercalcaemia as a result of bone metastasis or Kahler's disease, Kahler's disease.

Various: intense allergic reactions; as immunosuppressant in organ transplantation; as an adjuvant in the prevention of nausea and vomiting and in the treatment of cancer with oncolytics that have a serious emetic effect.

Childhood Croup:

Heterogeneous group of illnesses affecting the larynx, trachea and bronchi. Laryngotracheitis, laryngotracheobronchitis, laryngotracheobronchopneumonitis and spasmodic croup are included in the croup syndrome.

4.2 Posology and method of administration

Adults

General considerations:

The dosage should be titrated to the individual response and the nature of the disease. In order to minimise side effects, the lowest effective possible dosage should be used (see 'Side effects').

The initial dosage varies from 0.5 – 9mg a day depending on the disease being treated. In more severe diseases, doses higher than 9mg may be required. The initial dosage should be maintained or adjusted until the patient's response is satisfactory. Both the dose in the evening, which is useful in alleviating morning stiffness, and the divided dosage regimen are associated with greater suppression of the hypothalamo-pituitary-adrenal axis. If satisfactory clinical response does not occur after a reasonable period of time, discontinue treatment with dexamethasone and transfer the patient to another therapy.

If the initial response is favourable, the maintenance dosage should be determined by lowering the dose gradually to the lowest dose required to maintain an adequate clinical response. Chronic dosage should preferably not exceed 1.5mg dexamethasone daily.

Patients should be monitored for signs that may require dosage adjustment. These may be changes in clinical status resulting from remissions or exacerbations of the disease, individual drug responsiveness and the effect of stress (e.g. surgery, infection, trauma). During stress it may be necessary to increase dosage temporarily.

If the drug is to be stopped after more than a few days of treatment, it should be withdrawn gradually.

The following equivalents facilitate changing to dexamethasone from other glucocorticoids:

Milligram for milligram, dexamethasone is approximately equivalent to betamethasone, 4 to 6 times more potent than methylprednisolone and triamcinolone, 6 to 8 times more potent than prednisone and prednisolone, 25 to 30 times more potent than hydrocortisone, and about 35 times more potent than cortisone.

Acute, self-limiting allergic disorders or acute exacerbations of chronic allergic disorders.

The following dosage schedule combining parenteral and oral therapy is suggested:

First day: Dexamethasone sodium phosphate injection 4mg or 8mg (1ml or 2ml) intramuscularly.

Second day: 1mg (2.5ml) Dexamethasone Oral Solution twice a day.

| | |
|--------------|---|
| Third day: | 1mg (2.5ml) Dexamethasone Oral Solution twice a day. |
| Fourth day: | 500micrograms (1.25ml) Dexamethasone Oral Solution twice a day. |
| Fifth day: | 500micrograms (1.25ml) Dexamethasone Oral Solution twice a day. |
| Sixth day: | 500micrograms (1.25ml) Dexamethasone Oral Solution. |
| Seventh day: | 500micrograms (1.25ml) Dexamethasone Oral Solution. |
| Eighth day: | Re-assessment. |

If a dose of less than 5ml is required, an oral dosing device should be employed.

This schedule is designed to ensure adequate therapy during acute episodes whilst minimising the risk of overdosage in chronic cases.

Raised intracranial pressure: Initial therapy is usually by injection. When maintenance therapy is required, this should be changed to dexamethasone oral solution as soon as possible. For the palliative management of patients with recurrent or inoperable brain tumours, maintenance dosage should be calculated individually. A dosage of 2mg two or three times a day may be effective. The smallest dosage necessary to control symptoms should always be used.

Dexamethasone suppression tests:

1. Tests for Cushing's syndrome:

2mg (5ml) Dexamethasone Oral Solution should be administered at 11pm. Blood samples are then taken at 8am the next morning for plasma cortisol determination.

If greater accuracy is required, 500 micrograms (1.25ml) Dexamethasone Oral Solution should be administered every 6 hours for 48 hours. Blood should be drawn at 8am for plasma cortisol determination on the third morning.

24-hour urine collection should be employed for 17-hydroxycorticosteroid excretion determination.

2. Test to distinguish Cushing's syndrome caused by pituitary ACTH excess from the syndrome induced by other causes:

2mg (5ml) Dexamethasone Oral Solution should be administered every 6 hours for 48 hours. Blood should be drawn at 8am for plasma cortisol determination on the third morning.

24-hour urine collection should be employed for 17-hydroxycorticosteroid excretion determination.

Children:

Dosage should be limited to a single dose on alternate days to lessen retardation of growth and minimize suppression of hypothalamo-pituitary-adrenal axis.

Childhood Croup:

A single dose of 0.15mg/kg Dexamethasone Oral Solution is recommended. A second dose may be administered after 12 hours, if considered necessary by the treating physician.

Doses of up to 0.6mg/kg dexamethasone have been used safely in clinical studies. However, a maximum dose of 10mg (25ml Dexsol Oral Solution) is recommended.

The following dosage chart should be followed for the treatment of childhood croup at a dose of 0.15mg/kg.

| Approximate age (mths/yrs) | | Approximate weight (kg) | | Volume of Dexsol (ml) |
|-------------------------------|--------|----------------------------|-----|--------------------------|
| Min | Max | Min | Max | |
| 0 | 2 mths | 4 | 5.5 | 2 |
| 3 mths | 6 mths | 5.6 | 7.9 | 3 |

| | | | | |
|-----------|---------|------|------|----|
| 6 mths | 12 mths | 8 | 10.5 | 4 |
| > 12 mths | 2 yrs | 10.6 | 13.3 | 5 |
| > 2 yrs | 4 yrs | 13.4 | 16.2 | 6 |
| > 4 yrs | 7 yrs | 16.3 | 22 | 8 |
| > 7 yrs | 9 yrs | 22.1 | 27 | 10 |
| > 9 yrs | 12 yrs | 27.1 | 41 | 15 |
| > 12 yrs | 14 yrs | 42 | 55 | 20 |
| > 14 yrs | | 56 | 68 | 25 |

Elderly:

Treatment of elderly patients, particularly if long term, should be planned bearing in mind the more serious consequences of the common side effects of corticosteroids in old age.

4.3 Contraindications

- Hypersensitivity to dexamethasone or any of the excipients listed.
- Systemic infection unless specific anti-infective therapy is employed.
- Systemic fungal infections.
- Stomach ulcer or duodenal ulcer
- Infection with tropical worms

4.4 Special warnings and precautions for use

Patients should carry 'steroid treatment' cards, which give clear guidance on the precautions to be taken to minimise risk, and which provides details of prescriber, drug, dosage and the duration of treatment.

Undesirable effects may be minimised by using the lowest effective dose for the minimum period, and by administering the daily requirement as a single morning dose or whenever possible as a single morning dose on alternative days. Frequent patient review is required to appropriately titrate the dose against disease activity. When reduction in dosage is possible, the reduction should be gradual (Refer to 'Posology and Administration').

Anti-inflammatory/Immunosuppressive effects/Infection

Corticosteroids may exacerbate systemic fungal infections and should not be used unless they are needed to control drug reactions due to amphotericin. There have also been reports in which concomitant use of amphotericin and hydrocortisone was followed by cardiac enlargement and heart failure.

Administration of live virus vaccines is contra-indicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained.

Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may be atypical, and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.

Appropriate anti-microbial therapy should accompany glucocorticoid therapy when necessary e.g. in tuberculosis and viral and fungal infections of the eye.

There may be decreased resistance and inability to localise infection in patients on corticosteroids.

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 close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunisation with varicella/zoster

of herpes zoster, and if exposed they should seek urgent medical attention. Acute inflammation that necessitates immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous three months; this should be given within ten days of exposure to chickenpox. *If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.*

Measles can have a more serious or even fatal course in immunosuppressed patients. In such children or adults particular care should be taken to avoid exposure to measles. If exposed, prophylaxis with intramuscular pooled immunoglobulin (IG) may be indicated. Exposed patients should be advised to seek medical advice without delay.

Corticosteroids may activate latent amoebiasis or strongyloidiasis or exacerbate active disease. Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Amoeba, Candida, Cryptococcus, Mycobacterium, Nocardia, Pneumocystis or Toxoplasma. It is recommended that these are ruled out before initiating corticosteroid therapy particularly in those patients who have spent time in the tropics or those with unexplained diarrhoea.

A report shows that the use of corticosteroids in cerebral malaria is associated with a prolonged coma and an increased incidence of pneumonia and gastro-intestinal bleeding and therefore corticosteroids should not be used in cerebral malaria.

Eye disorders

Prolonged use of corticosteroids may produce subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses. Particular care is needed when treating patients with glaucoma (or family history of glaucoma) as well as when treating patients with ocular herpes simplex, because of possible corneal perforation.

Electrolyte disturbances

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, retention of salt and water, and increased excretion of potassium, but these effects are less likely to occur with synthetic derivatives, except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary with corticosteroid therapy. All corticosteroids increase calcium excretion.

Particular care is needed when treating patients with renal impairment, hypertension and congestive heart failure.

Adrenal Suppression

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must therefore always be gradual to avoid acute 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 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 corticosteroids may be reduced rapidly to physiological doses. Once a daily dose of 1mg dexamethasone is reached, dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse.

Abrupt withdrawal of doses of up to 6 mg daily of dexamethasone for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression in the majority of patients.

In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

- Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.
- When a short course has been prescribed within one year of cessation of long term therapy (months or years).
- Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy.
- Patients receiving doses of systemic corticosteroid greater than 6 mg daily of dexamethasone.
- Patients repeatedly taking doses in the evening.

Intercurrent illness and stress

During prolonged therapy, any intercurrent illness, trauma, stress or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Patients under stress may require increased doses of corticosteroids prior, during and after the period of stressful situation.

Withdrawal symptoms

Stopping corticosteroids after prolonged therapy may cause withdrawal symptoms including fever, myalgia, arthralgia and malaise. This may occur in patients even without evidence of adrenal insufficiency.

General

In addition to the information given under the other headings, particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary:

- diabetes mellitus (or a family history of diabetes)
- osteoporosis (especially post-menopausal females)
- previous corticosteroid-induced myopathy
- myasthenia gravis
- non-specific ulcerative colitis, diverticulitis or fresh intestinal anastomosis
- peptic ulceration
- liver failure
- epilepsy
- migraine
- history of allergy to corticosteroids
- herpes simplex

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Fat embolism has been reported as a possible complication of hypercortisonism.

Large doses of corticosteroids may mask the symptoms of gastro-intestinal perforation.

Reports in the literature suggest an apparent association between use of corticosteroids and left-ventricular free-wall rupture after a recent myocardial infarction; therefore, corticosteroids should be used with great caution in these patients.

In rare cases, decrease or withdrawal of orally administered corticosteroids could reveal underlying disease that is accompanied by eosinophilia (e.g. Churg Strauss Syndrome) in patients with asthma.

Hypersensitivity

Rare cases of anaphylactoid or hypersensitivity reactions such as glottis oedema, urticaria and bronchospasm have been reported especially with parenteral administration of corticosteroids and in patients with a history of allergy. Prophylactic measures should be taken especially if the patient has a history of allergic reactions to medicines.

If such anaphylactoid reaction occurs, the following measures are recommended:

immediate slow intravenous injection of 0.1-0.5ml of adrenaline (solution of 1:1000:0.1-0.5mg adrenaline dependent on body weight), intravenous administration of aminophylline and artificial respiration if necessary.

Psychiatric reactions

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.

Use in Children and Adolescents

Corticosteroids cause growth retardation. On prolonged administration glucocorticoids may accelerate epiphyseal closure.

Treatment should be limited to the minimum dose for the shortest period.

Children and adolescents on prolonged therapy should be carefully monitored.

Preterm neonates

Excipient Warnings.

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.

Use in the Elderly

The common adverse effects 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. Close clinical supervision is required to avoid life-threatening reactions.

Excipient Warnings

This product contains:

- Propylene glycol – This may cause alcohol like symptoms
- Liquid maltitol and sorbitol – Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicinal products on dexamethasone:

Dexamethasone is metabolized via cytochrome P450 3A4 (CYP3A4). Concomitant administration of dexamethasone with inducers of CYP3A4, such as phenytoin, barbiturates (e.g. primidone and phenobarbital), ephedrine, rifabutin, carbamazepine and rifampicin may lead to decreased plasma concentrations of dexamethasone and the dose may need to be increased.

Dexamethasone reduces the plasma concentration of the antiviral drugs indinavir and saquinavir.

Patients taking methotrexate and dexamethasone have an increased risk of haematological toxicity.

Concomitant administration of inhibitors of CYP3A4 such as ketoconazole, ritonavir and erythromycin may lead to increased plasma concentrations of dexamethasone.

These interactions may also interfere with dexamethasone suppression tests, which therefore should be interpreted with caution during administration of substances that affect the metabolism of dexamethasone.

Ketoconazole may increase plasma concentrations of dexamethasone by inhibition of CYP3A4, but may also suppress corticosteroid synthesis in the adrenal and thereby cause adrenal insufficiency at withdrawal of corticosteroid treatment.

Ephedrine may increase the metabolic clearance of corticosteroids, resulting in decreased plasma levels. An increase of the corticosteroid dose might be necessary.

False-negative results in the dexamethasone suppression test in patients being treated with indometacin have been reported.

Antibiotics: Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance

Anticholinesterases: Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

Colestyramine: Colestyramine may decrease the absorption of dexamethasone.

Estrogens, including oral contraceptives: Estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect

Aminoglutethimide: Decrease of dexamethasone efficacy, due to its metabolism increase. An adjustment of dexamethasone dosage may be required.

Gastrointestinal topicals, antacids, charcoal: A decrease in digestive absorption of glucocorticoids have been reported with prednisolone and dexamethasone. Therefore, glucocorticoids should be taken separately from gastrointestinal topicals, antacids or charcoal, with an interval between treatment of at least two hours.

Effects of dexamethasone on other medicinal products

Dexamethasone is a moderate inducer of CYP3A4. Concomitant administration of dexamethasone with substances that are metabolised via CYP3A4 could lead to increased clearance and decreased plasma concentrations of these substances.

The renal clearance of salicylates is increased by corticosteroids and therefore, salicylate dosage should be reduced along with steroidal withdrawal.

The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids.

The hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, amphotericin B injection, potassium depleting agents, corticosteroids (gluco-mineralo), tetracosactide and carbenoxolone are enhanced. Hypokalaemia predisposes to cardiac arrhythmia especially "torsade de pointes" and increase the toxicity of cardiac glycosides. Hypokalemia should be corrected before corticosteroid treatment initiation. In addition, there have been cases reported in which concomitant use of

corrected before corticosteroid treatment initiation. In addition, there have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.

Sultopride has been linked to ventricular arrhythmias, especially torsade de pointes. This combination is not recommended.

Patients taking NSAID's should be monitored since the incidence and/or severity of gastro-ulceration may increase. Aspirin should also be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

Antitubercular drugs: Serum concentrations of isoniazid may be decreased.

Cyclosporin: Increased activity of both cyclosporin and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

Thalidomide: Co-administration with thalidomide should be employed cautiously, as toxic epidermal necrolysis has been reported with concomitant use.

Corticosteroids may affect the nitrobulletetrazolium test for bacterial infection and produce false-negative results.

Vaccines attenuated live

Risk of fatal systemic disease

Praziquantel:

Decrease in praziquantel plasmatic concentrations, with a risk of treatment failure, due to its hepatic metabolism increased by dexamethasone.

Oral anticoagulants:

Possible impact of corticosteroid therapy on the metabolism of oral anticoagulants and on clotting factors. At high doses or with treatment for more than 10 days, there is a risk of bleeding specific to corticosteroid therapy (gastrointestinal mucosa, vascular fragility). Patients taking corticosteroids associated with oral anticoagulants should be closely monitored (biological investigations on 8th day, then every 2 weeks during treatment and after treatment discontinuation)

Insulin, sulfonylureas, metformin:

Increase in blood glucose, with sometimes diabetic ketosis, since corticosteroids impair carbohydrate tolerance. Therefore, blood and urine self-monitoring should be reinforced by the patient, in particular at the start of treatment

Isoniazid:

A decrease in plasma isoniazid levels have been reported with prednisolone. The suggested mechanism is an increase in hepatic metabolism of isoniazid and a decrease in the hepatic metabolism of isoniazid and a decrease in the hepatic metabolism of glucocorticoids. Patients taking isoniazid should be closely monitored.

4.6 Use during pregnancy and lactation

Since adequate human reproduction studies have not been performed with corticosteroids, dexamethasone should not be used during pregnancy for maternal indications, unless it is clearly necessary. The lowest effective dose needed to maintain adequate disease control should be used.

Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Patients with pre-eclampsia or fluid retention require close monitoring.

Placental transfer in considerable: foetal serum concentrations are similar to maternal concentrations.

Corticosteroids are excreted in small amounts in breast milk and may suppress growth, interfere with endogenous corticosteroid production or cause other unwanted effects. A decision on whether to continue/discontinue breast feeding or to continue/discontinue therapy with dexamethasone should be made taking into account the benefit of breast feeding to the child and the benefit of dexamethasone therapy to the woman.

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.

4.7 Effects on ability to drive and use machines

There are some side effects associated with this product that may affect some patients' ability to drive or operate machinery (see 4.8 Undesirable effects).

4.8 Undesirable effects

The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment (refer to Special Warnings and Precautions).

The following side effects have been reported; there frequency is unknown.

| System Organ Class | |
|--|---|
| Infections and infestations | Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis. Decreased resistance to infection |
| Blood and lymphatic system disorders | Leucocytosis |
| Immune system disorders | Hypersensitivity including anaphylaxis has been reported. |
| Endocrine disorders | Menstrual irregularities and amenorrhoea, suppression of the hypothalamic-pituitary-adrenal axis, premature epiphyseal closure, development of Cushingoid state, hirsutism, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery or illness). Negative protein and calcium balance. |
| Metabolism and nutrition disorders | Sodium retention, fluid retention, potassium loss, hypokalaemic alkalosis, increased calcium excretion. Increased appetite. Impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy. |
| Nervous system disorders | <p>Convulsions and aggravation of epilepsy, vertigo, headache, increased intra-cranial pressure with papilloedema in children (Pseudotumour cerebri), usually after treatment withdrawal, psychological dependence, depression, insomnia, aggravation of schizophrenia and psychic disturbances ranging from euphoria to frank psychotic manifestations.</p> <p>A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.</p> |
| Eye disorders | Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, papilloedema, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases, exophthalmos. |
| Cardiac disorders | congestive heart failure in susceptible patients |
| Vascular disorders | Thromboembolism, hypertension |
| Gastrointestinal disorders | Dyspepsia, peptic ulceration with perforation and haemorrhage, acute pancreatitis, candidiasis. Abdominal distension and vomiting. Ulcerative oesophagitis. Perforation of the small and large bowel particularly in patients with inflammatory bowel disease. Nausea, hiccups. |
| Skin and subcutaneous tissue disorders | Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, striae, telangiectasia, acne, increased sweating, suppressed reaction to skin tests, other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic oedema, thinning scalp hair. |
| Musculoskeletal and connective | Osteoporosis, vertebral and long bone fractures, avascular necrosis, tendon rupture. |

| | |
|--|---|
| tissue disorders | Proximal myopathy. Muscle weakness, aseptic necrosis of femoral and humeral heads, loss of muscle mass. Growth suppression in children and adolescents. |
| General disorders and administration site conditions | Malaise, abnormal fat deposits. |
| Investigations | Increased or decreased motility and number of spermatozoa, weight gain. |

Withdrawal symptoms and signs

Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (See 'Special Warnings and Precautions').

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

4.9 Overdose

Reports of acute toxicity and/or deaths following overdosage with glucocorticoids are rare. No antidote is available. Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him unusually susceptible to ill effects from corticosteroids. In this case, the stomach should be emptied and symptomatic treatment should be instituted as necessary. Anaphylactic and hypersensitivity reactions may be treated with epinephrine (adrenaline), positive-pressure artificial respiration and aminophylline. The patient should be kept warm and quiet. The biological half life of dexamethasone in plasma is about 190 minutes.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC Code: H02AB02

Pharmacotherapeutic Group: Corticosteroid

Dexamethasone is a highly potent and long-acting glucocorticoid with negligible sodium retaining properties and is therefore, particularly suitable for the use in patients with cardiac failure and hypertension. Its anti-inflammatory potency is 7 times greater than prednisolone and like other glucocorticoids, dexamethasone also has anti-allergic, antipyretic and immunosuppressive properties.

Dexamethasone has a biological half life of 36 - 54 hours and therefore is suitable in conditions where continuous glucocorticoid action is required.

5.2 Pharmacokinetic properties

Dexamethasone is well absorbed when given by mouth; peak plasma levels are reached between 1 and 2 hours after ingestion and show wide interindividual variations. The mean plasma half life is 3.6 ± 0.9 h. Dexamethasone is bound (to about 77%) to plasma proteins, mainly albumins. Percentage protein binding of dexamethasone, unlike that of cortisol, remains practically unchanged with increasing steroid concentrations. Corticosteroids are rapidly distributed to all body tissues. Dexamethasone is metabolised mainly in the liver but also in the kidney. Dexamethasone and its metabolites are excreted in 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, inter-uterine growth can be delayed. All these effects were seen at high doses.

6. Pharmaceutical particulars

6.1 List of excipients

Benzoic acid, propylene glycol, citric acid monohydrate, liquid maltitol, garden mint flavour (containing isopropanol and propylene glycol), liquid sorbitol non-crystallising, sodium citrate and purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Shelf Life: 2 years

Shelf life after first opening the container: 3 months

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate.

The storage at temperatures higher than 25°C could allow precipitation inside the solution. Do not use the product if solid particles are observed inside the solution.

This product is sensitive to light. Store in the original package.

6.5 Nature and contents of container

Bottles: 75ml and 150ml in Amber (Type III) glass.

Closures: HDPE, EPE wadded, tamper evident, child resistant closure.

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing authorisation holder

Rosemont Pharmaceuticals Ltd., Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE, UK

8. Marketing authorisation number(s)

PL 00427/0137

9. Date of first authorisation/renewal of the authorisation

Date of first authorisation: 08th March 2005

10. Date of revision of the text

12 April 2013