Formulary decision guide: Dexamethasone 2 mg/5 ml oral solution (Dexsol®)

Guidelines in practice

Product current status:		
Product proposed status:		
Date of next meeting:		
Decision:	**Yes**	**No**
Restricted use:		

Drug name

Dexamethasone 2 mg/5 ml oral solution (Dexsol®)

Indications

- In addition to other current indications (see summary of product characteristics),[1] dexamethasone liquid (Dexsol®) is now indicated for childhood croup
- It is suitable for patients unable/unwilling to swallow dexamethasone tablets or capsules.

Dosage

- Oral administration of dexamethasone is preferred in the case of croup, as there is evidence that it is at least as effective as intramuscular dexamethasone[2]
- Give all children with mild, moderate, or severe croup a single dose of oral dexamethasone (0.15 mg/kg body weight). If it is not possible to weigh the child, as a rough guide the dose would be 1.5–2.0 mg for an average-sized child aged 12–15 months and 2–3 mg for an average-sized child aged 3–4 years[2]
- Please refer to the summary of product characteristics.[1]

Mode of action

- Corticosteroids such as dexamethasone form a class of naturally occurring chemicals that includes steroid hormones, which are produced in the adrenal cortex.

Evidence for use

- There is good evidence that corticosteroids are beneficial in children with mild, moderate, and severe croup[2]
- Dexamethasone is effective in relieving the symptoms of croup as early as 6 hours after treatment. Fewer co-interventions are used and hospital stays are decreased for patients treated with glucocorticoids[3]
- A single oral dose of dexamethasone proved more effective than a single oral dose of prednisolone in reducing unscheduled re-presentation to medical care in children with mild to moderate croup[4]
- More severe croup (or mild croup that might cause complications) calls for hospital admission:[5]
  - a single dose of corticosteroid should be administered before transfer to hospital
  - in hospital, treatment with a corticosteroid or nebuliser will often reduce symptoms—the dose may be repeated after 12 hours if necessary
- Providers of urgent care services should ensure that dexamethasone is available.[2]

Cost effectiveness

- For children with mild croup, dexamethasone is an effective treatment that results in consistent and small but important clinical and economic benefits, and, although the long-term effects of this treatment are not known, data support the use of dexamethasone in most, if not all, children with croup.[6]

Contraindications

- Possible contraindications are:[1]
  - 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.

Precautions and side effects

- Please refer to the summary of product characteristics.[1]

References

1. Rosemont Pharmaceuticals Ltd. *Dexsol 2 mg/5 ml. Summary of Product Characteristics*. November 2012.
2. NHS Evidence. *Clinical Knowledge Summaries: Croup management*. www.cks.nhs.uk/croup#-335627
3. NHS National Institute for Health Research. The effectiveness of glucocorticoids in treating croup: meta-analysis. York: Centre for Reviews and Dissemination, 2000. Available at: www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=11999009674
4. Sparrow A, Geelhoed G. Prednisolone versus dexamethasone in croup: a randomised equivalence trial. *Arch Dis Child* 2006; **91**: 580–583. doi: 10.1136/adc.2005.089516
5. Paediatric Formulary Committee. *BNF for Children* (online). London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. Available at: www.medicinescomplete.com [Accessed February 2013.]
6. Bjornson C, Johnson D. Croup. *Lancet* 2008; **371**(9609): 329–339.

Key points

- Dexamethasone oral solution may benefit:
  - children with croup—swallowing tablets or capsules or other solid-dose medications may be difficult
  - patients who require this medicine, but who have transient swallowing difficulties.

This formulary decision guide was developed from content provided by Rosemont Pharmaceuticals Ltd in a format developed by *Guidelines in Practice*. It has been reviewed by a member of the *Guidelines in Practice* editorial board. At all times editorial control has remained with *Guidelines in Practice*.

Abbreviated prescribing information can be found overleaf

Product code: DTM033

Rosemont® The source of liquid solutions.

Date of preparation: March 2014

Formulary decision guide: Dexamethasone 2 mg/5 ml oral solution (Dexsol®)

Guidelines in practice

Abbreviated Prescribing Information: DEXSOL 2mg/5ml. Consult Summary of Product Characteristics before prescribing.

Presentation: Solution containing 2mg Dexamethasone (as sodium phosphate) in each 5ml. **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. Childhood Croup: Heterogeneous group of illnesses affecting the larynx, trachea and bronchi. Laryngotracheitis, laryngotracheobronchitis, laryngotracheobronchopneumonitis and spasmodic croup are included in the croup syndrome. **Posology:** Adults: The dosage should be titrated to the individual response and the nature of the disease. The lowest effective possible dosage should be used. The initial dosage varies from 0.5 – 9mg a day. In more severe diseases, doses higher than 9mg may be required. If satisfactory response does not occur after a reasonable time, discontinue treatment and transfer the patient to another therapy. Chronic dosage should preferably not exceed 1.5mg daily. If the drug is to be stopped after more than a few days of treatment, it should be withdrawn gradually. Children: Dosage should be limited to a single dose on alternate days. **Childhood Croup:** A single dose of 0.15mg/kg is recommended. A second dose may be administered after 12 hours, if considered necessary by the treating physician. However, a maximum dose of 10mg) is recommended. Elderly: Care should be taken. **Contra-indications:** Hypersensitivity to dexamethasone or any of the excipients. Systemic infection unless specific anti-infective therapy is employed. Systemic fungal infections. Stomach or duodenal ulcer. Infection with tropical worms. **Precautions for use:** Patients should carry 'steroid treatment' cards. Corticosteroids should only be used in systemic fungal infections to control drug reactions due to amphotericin. If inactivated viral or bacterial vaccines are administered 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 may be masked and reach an advanced stage before being recognised. Appropriate anti-microbial therapy should accompany glucocorticoid therapy when necessary. There may be decreased resistance and inability to localise infection in patients on corticosteroids. Chickenpox and measles are of particular concern, since these normally minor illnesses may be fatal in immunosuppressed patients. In such children or adults particular care should be taken to avoid exposure. Exposed patients should be advised to seek medical advice without delay. Corticosteroids may activate latent infections or exacerbate active disease due to pathogens. Prolonged use 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. Should not be used in cerebral malaria. Salt restriction and potassium supplementation may be necessary. Calcium excretion will be increased. Adrenal cortical atrophy develops during prolonged therapy. Withdrawal after prolonged therapy must always be gradual. 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 prior, during and after the period of stressful situation. 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. There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis. Particular care is required in patients with the following conditions: renal insufficiency, hypertension or congestive heart failure, diabetes mellitus (or a family history of diabetes), osteoporosis, previous corticosteroid-induced myopathy, glaucoma (or family history of glaucoma), myasthenia gravis, non-specific ulcerative colitis, diverticulitis or fresh intestinal anastomosis, peptic ulceration, existing or previous history of severe affective disorders (especially previous steroid psychosis), liver failure, epilepsy, migraine, history of allergy to corticosteroids, tuberculosis, herpes simplex, psychiatric disorders. Fat embolism has been reported as a possible complication of hypercortisonism. Large doses may mask the symptoms of gastro-intestinal perforation. Use with great caution after recent myocardial infarction. Decrease or withdrawal could reveal underlying diseases that are accompanied by eosinophilia in patients with asthma. Potentially severe psychiatric adverse reactions may occur. Seek medical advice if worrying psychological symptoms develop (especially depressed mood or suicidal ideation). Particular care is required in patients with or having close relatives with existing history of severe affective disorders. Children on prolonged therapy should be carefully monitored for growth retardation. Preterm neonates: Evidence of long-term neurodevelopmental adverse events after early treatment (<96 hours) in chronic lung disease. **Excipient Warnings:** Propylene glycol – This may cause alcohol like symptoms. It also contains 0.7g sorbitol in each 5ml. It is unsuitable in hereditary fructose intolerance and can cause stomach upset and diarrhoea. It also contains liquid maltitol which may cause diarrhoea. **Drug interactions:** Dexamethasone is metabolized via cytochrome P450 3A4 (CYP3A4). 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 with inducers of CYP3A4 may lead to decreased plasma concentrations. Concomitant administration of inhibitors of CYP3A4 may lead to increased plasma concentrations. These interactions may also interfere with dexamethasone suppression tests. Ketoconazole may cause adrenal insufficiency at withdrawal of corticosteroid treatment. Ephedrine may decrease plasma levels. False-negative results in the dexamethasone suppression test inpatients being treated with indometacin have been reported. Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance. Concomitant use of anticholinesterase agents may produce severe weakness in patients with myasthenia gravis. Colestyramine may decrease the absorption of dexamethasone. Estrogens may increase the effect of corticosteroids. Aminoglutethimide decreases dexamethasone efficacy. Glucocorticoids should be taken separately from gastrointestinal topicals, antacids or charcoal. 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. The effects of hypoglycaemic agents, anti-hypertensives and diuretics are antagonised. The hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, amphotericin B, potassium depleting agents, corticosteroids (gluco-mineralo), tetracosactide and carbenoxolone are enhanced. Hypokalemia should be corrected before corticosteroid treatment initiation. Concomitant use of amphotericin B and hydrocortisone has been followed by cardiac enlargement and congestive heart failure. Concomitant sultopride and dexamethasone is not recommended. Patients taking NSAID's should be monitored. Aspirin should also be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia. Serum isoniazid may be decreased. Increased activity of both ciclosporin and corticosteroids may occur. Co-administration with thalidomide should be employed cautiously. Corticosteroids may affect the nitrobuletetrazolium test for bacterial infection and produce false-negative results. Risk of fatal systemic disease with attenuatedlive vaccines. Decrease in praziquantel plasma concentrations, with a risk of treatment failure. Possible impact of corticosteroid therapy on the metabolism of oral anticoagulants and on clotting factors. Glucose control in diabetics may be impaired. **Pregnancy and lactation:** Dexamethasone should not be used during pregnancy for maternal indications, unless it is clearly necessary. 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. Foetal serum concentrations are similar to maternal concentrations. Corticosteroids are excreted in small amounts in breast milk. **Effects on ability to drive and use machines:** Ability to drive or operate machinery may be affected. **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. Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis, hypertension, increased calcium excretion. Osteoporosis, vertebral and long bone fractures, avascular necrosis, tendon rupture. Proximal myopathy. Muscle weakness, aseptic necrosis of femoral and humeral heads, loss of muscle mass. 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. 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. Posterior subcapsular cataracts, increased intra-ocular pressure, glaucoma, papilloedema, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases, exopthalmos. Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis. Decreased resistance to infection. Menstrual irregularities and amenorrhoea, growth suppression in children and adolescents, premature epiphyseal closure, development of Cushingoid state, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy. Negative protein and calcium balance. Secondary adrenocortical and pituitary unresponsiveness. Convulsions and aggravation of epilepsy, vertigo, headache, increased intra-cranial pressure with papilloedema in children, psychological dependence, depression, insomnia, aggravation of schizophrenia and psychic disturbances. Affective disorders, psychotic reactions, behavioural disturbances, anxiety, cognitive dysfunction. Hypersensitivity including anaphylaxis. Leucocytosis, thromboembolism, increased appetite, nausea, malaise, hiccups, abnormal fat deposits, increased or decreased motility and number of spermatozoa. Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight. **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. **Shelf Life and Storage:** 2 years unopened (3 months after opening). Do not store above 25°C. Do not refrigerate. This product is sensitive to light. Store in the original package. **Legal Category:** POM **Pack Size and NHS Price:** 75ml - £21.51 and 150ml - £42.30. **Marketing Authorisation Holder:** Rosemont Pharmaceuticals Ltd, Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds, LS11 9XE. **Marketing Authorisation Number:** PL00427/0137. **Date of Preparation:** April 2013

Information about adverse event reporting can be found at www.yellowcard.gov.uk.

Adverse events should also be reported to Rosemont Pharmaceuticals Ltd on 0113 244 1400