1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

BETADEXAMINE (liquid)

COMPOSITION

Each 5 ml of BETADEXAMINE liquid contains:

Betamethasone	0,25 mg
Dexchlorpheniramine maleate	2,00 mg

Excipients:

Colour sunset yellow (C.I. 15985), citric acid monohydrate, disodium edetate, flavor peach, glycerol, polysorbate 80, propylene glycol, purified water, saccharin sodium, sodium benzoate, sodium chloride, sorbitol solution 70 %

Preservative:

Sodium benzoate	0,1 % *m/v*

Contains sugar: Sorbitol solution (70 %)	2,00 g

Contains sweetener: Saccharin sodium	3,50 mg

CATEGORY AND CLASS

A 21.5.4 Corticosteroid combinations

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

BETADEXAMINE is a combination of betamethasone and dexchlorpheniramine and has antihistaminic and anti-inflammatory properties.

Pharmacokinetic properties

Betamethasone 0,25 mg is therapeutically equivalent to 1,6 mg of prednisone and has a pharmacological half-life of 5 to 6 hours but a biological active half-life of 36 to 72 hours. After oral administration, it is 72 % bioavailable. Betamethasone has a slightly less mineralocorticoid (salt retention) effect.

Dexchlorpheniramine has a mean half-life of 30 hours (shorter in children) and after oral administration it is 25 to 50 % bioavailable.

INDICATIONS

BETADEXAMINE is indicated as a second-line therapy when antihistamines are not effective for the treatment of:

- Short-term treatment of allergic rhinitis
- Steroid-responsive dermatological allergies and steroid-responsive dermatoses.

CONTRAINDICATIONS

BETADEXAMINE is contraindicated in patients with:

- Hypersensitivity to dexchlorpheniramine or racemic chlorphenamine, betamethasone or any of the excipients for BETADEXAMINE (see COMPOSITION).
- Newborn and premature infants. This age group has an increased susceptibility to anticholinergic side effects including central nervous system (CNS) excitation, and an increased tendency towards convulsions.
- Patients receiving monoamine oxidase inhibitors (MAOI) or within two weeks after use of a

MAOI. Concurrent use with BETADEXAMINE may prolong and intensify the anticholinergic and CNS depressant effects (see INTERACTIONS).

- Systemic fungal infections.
- Children below the age of 12 years as safety has not been established.
- Glaucoma.

WARNINGS AND SPECIAL PRECAUTIONS

BETADEXAMINE contains a potent, long-acting corticosteroid.

The recommended maximum treatment period should not be exceeded.

Long term use of corticosteroids such a BETADEXAMINE, particularly in high doses and in young children can lead to suppression of the HPA axis. This may lead to Cushingoid signs, growth and development retardation in children and increased susceptibility to stress and adrenal crisis in all patients (see CONTRAINDICATIONS).

Patients undergoing stress, such as major surgery, septicaemia or trauma, who have signs of HPA axis suppression, should receive replacement therapy to prevent a possible adrenal crisis.

Corticosteroids, such as BETADEXAMINE, should be used with caution in ulcerative colitis, increased intraocular pressure, active or latent peptic ulcer, abscess or other pyogenic infections, active tuberculosis, systemic fungal infections, renal failure, hypertension, osteoporosis, hyperthyroidism, cirrhosis, ocular herpes simplex infection and glaucoma, diverticulitis, fresh intestinal anastomoses, myasthenia gravis, congestive heart failure, patients with diabetes mellitus and elderly patients.

BETADEXAMINE may aggravate existing emotional instability or psychotic tendencies.

With corticosteroid therapy such as BETADEXAMINE, dietary salt restriction and potassium supplementation may be considered. BETADEXAMINE increases calcium excretion.

Prolonged BETADEXAMINE use may produce posterior subcapsular cataracts and glaucoma, and may enhance secondary ocular infections due to fungi or viruses.

BETADEXAMINE therapy may mask some signs of infection.

BETADEXAMINE may decrease blood salicylate concentrations.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinaemia.

Whilst on BETADEXAMINE therapy patients should not be vaccinated against smallpox. Other immunisation procedures should not be undertaken in patients receiving BETADEXAMINE, especially those receiving high doses.

Thromboembolic complications and muscular weakness have been reported.

BETADEXAMINE should be used with caution in patients with active or latent peptic ulcer, pyloroduodenal obstruction, prostatic hypertrophy or bladder neck obstruction, cardiovascular disease including hypertension, and in patients with hyperthyroidism.

BETADEXAMINE should be avoided in patients with narrow angle glaucoma (see CONTRAINDICATIONS).

Antihistamines, as contained in BETADEXAMINE, may cause dizziness, sedation and hypotension, especially in patients over 60 years of age.

Incoordination can occur with antihistamines such as BETADEXAMINE, although paradoxical stimulation may occasionally occur, especially at high doses and in children or the elderly.

Reports of convulsions in patients taking BETADEXAMINE suggest a need for caution in patients with epilepsy.

Effects on ability to drive and operate machines

BETADEXAMINE may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be warned against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

Excipients

Patients with the rare hereditary condition of sorbitol intolerance should not take BETADEXAMINE.

BETADEXAMINE contains sorbitol and may have a laxative effect.

INTERACTIONS

Dosage and therapeutic effects should be monitored closely when BETADEXAMINE is used concurrently with:

- Monoamine oxidase inhibitors may exacerbate the CNS depressant and anticholinergic effects of the dexchlorpheniramine in BETADEXAMINE.
- Phenobarbitone, phenytoin, rifampicin or ephedrine, as these can cause a reduced steroid effect.
- Oestrogen as this can cause an increased steroid effect.
- Potassium-depleting diuretic, digoxin and amphotericin B can cause increased hypokalaemia.
- Anticoagulants such as warfarin can cause an increase in PTT (increased INR).

- Nonsteroidal anti-inflammatory medicines can aggravate the ulcerogenic effect of betamethasone.
- Antidiabetic medicines, oral and insulin, may require a dosage adjustment of both medicines as betamethasone may increase blood glucose concentration.
- Other oral anticoagulants as these can result in either a decrease in anticoagulant effect due to dexchlorpheniramine, or in an increased anticoagulant effect due to the betamethasone. Close monitoring of the international normalized ratio (INR) or prothrombin time (PT) is required.
- Alcohol, tricyclic antidepressants, barbiturates or other central nervous system depressants may potentiate the sedative effect of BETADEXAMINE.
- Medicines with anticholinergic effects will potentiate the sedative effects of BETADEXAMINE.
- Corticosteroids, such as BETADEXAMINE, may decrease blood salicylate concentrations. Aspirin should be used cautiously in conjunction with BETADEXAMINE in hypoprothrombinaemia.
- Whilst on BETADEXAMINE therapy patients should not be vaccinated against smallpox or with live attenuated virus vaccines. Other immunisation procedures should not be undertaken in patients receiving corticosteroids, especially those receiving high doses.
- Concomitant glucocorticoid therapy may inhibit the response to somatotropin.

HUMAN REPRODUCTION

Safety and efficacy in pregnancy and lactation have not been established (see CONTRAINDICATIONS).

Infants born to mothers who had high doses of BETADEXAMINE during pregnancy should be carefully monitored for signs of hypoadrenalism.

Fertility

Corticosteroid therapy, such as BETADEXAMINE, may alter the motility and number of spermatozoa.

DOSAGE AND DIRECTIONS FOR USE

Dosage should be individualised and adjusted according to the condition under treatment and the response obtained.

BETADEXAMINE is only to be used for short-term treatment (less than 5 days).

BETADEXAMINE should only be used for well-defined indications.

BETADEXAMINE should not be mixed with other mixtures.

Adults and children over 12 years of age:

Recommended initial dose: Take 5 ml to 10 ml four times daily, after meals and at bedtime.
The dose should not exceed 40 ml daily.

The dose should be tapered off and discontinued as improvement occurs.

Treatment should not exceed 5 days.

The course should not be repeated within 28 days unless specifically indicated by a medical practitioner.

Not for use in children under 12 years of age.

Shake bottle before use.

SIDE EFFECTS

Betamethasone

Immune system disorders

Frequent: Increased risk of infection

Less frequent: Generalised allergic reactions

Endocrine disorders

Frequent: Decreased body growth

Less frequent: Cushing's syndrome, hyperglycaemia, adrenocortical insufficiency

Metabolism and nutrition disorders

Less frequent: Sodium and fluid retention, negative protein, nitrogen and calcium balance, hypokalaemia

Psychiatric disorders

Frequent: Depression, euphoria

Nervous system disorders

Less frequent: Nervousness, restlessness

Eye disorders

Less frequent: Cataracts, glaucoma

Cardiac disorders

Frequent: Hypertension

Respiratory, thoracic and mediastinal disorders

Less frequent: Pulmonary tuberculosis

Gastrointestinal disorders

Frequent: Gastric irritation, nausea, vomiting, dyspepsia, increased appetite, indigestion, pancreatitis

Less frequent: Peptic ulcer

Skin and subcutaneous tissue disorders

Frequent: Atrophic condition of the skin, impaired skin healing

Musculoskeletal, connective tissue and bone disorders

Less frequent: Osteoporosis

Renal and urinary disorders

Less frequent: Fluid and electrolyte disturbances

Dexchlorpheniramine

Blood and lymphatic system disorders

Less frequent: Agranulocytosis, thrombocytopenia, pancytopenia, aplastic anaemia, leucopenia, haemolytic anaemia

Immune system disorders

Less frequent: Hypersensitivity reactions (including bronchospasm, angioedema, and anaphylaxis)

Psychiatric disorders

Less frequent: Depression

Nervous system disorders

Frequent: Somnolence, slight drowsiness to sleep, lassitude, dizziness, incoordination, headache, psychomotor impairment

Less frequent: Convulsions, tremor, sleep disturbances, confusion, paraesthesia, neuritis, extrapyramidal effects

Eye disorders

Frequent: Blurred vision

Ear and labyrinth disorders

Less frequent: Tinnitus

Cardiac disorders

Less frequent: Cardiac dysrhythmias, palpitations, hypotension

Respiratory, thoracic and mediastinal disorders

Frequent: Thickening of the mucus, dry nasal mucosa

Gastrointestinal disorders

Frequent: Constipation and increased gastric reflux, xerostomia

Less Frequent: Nausea, vomiting, diarrhoea, epigastric pain

Hepato-biliary disorders

Less frequent: Jaundice

Skin and subcutaneous tissue disorders

Less frequent: Rash, hair loss, sweating, urticaria

Musculoskeletal, connective tissue and bone disorders

Less frequent: Myalgia

Renal and urinary disorders

Frequent: Urinary difficulty or retention

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Symptoms

Betamethasone

(see SIDE EFFECTS).

Dexchlorpheniramine

Overdosage with sedating antihistamines is associated with antimuscarinic, extrapyramidal, and CNS effects. When CNS stimulation predominates over CNS depression, which is more likely in children or the elderly, it causes ataxia, excitement, tremors, psychoses, hallucinations, and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma, and convulsions, progressing to respiratory failure and cardiovascular collapse.

Treatment

Treatment is symptomatic and supportive.

IDENTIFICATION

A bright, clear orange solution with a fruity peach odour

PRESENTATION

100 ml round, amber, glass bottle with white, tamper-evident, polypropylene screw cap. The bottle is placed in an outer cardboard carton together with a leaflet

100 ml, high density polyethylene, brown bottle with a white, low density polyethylene, snap-cap

closure. The bottle is placed in an outer cardboard carton together with a leaflet

Not all packs are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C, in well-closed containers.

Protect from light

Keep in original package until required for use

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

A40/21.5.4/0623

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

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DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION

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