NALIS® DEXAMETHASONE SYRUP.

(DEXAMETHASONE BP 0.5MG/5ML)

SUBMITTED BY: NALIS PHARMACEUTICALS LTD

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SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC) .

1. NAME OF THE DRUG PRODUCT

Nalis Dexamethasone Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

A red colored solution with strawberry flavor.

Each ml of solution contains

Dexamethasone (as dexamethasone sodium phosphate)…… 0.5 mg

Excipients…….. q.s

3. PHARMACEUTICAL FORM

Oral Solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Nalis Dexamethasone Syrup 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, Sjögrens 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.

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.

4.2 Posology and method of administration

Posology

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 2mg/5ml Oral Solution twice a day.**
Third day:	**1mg (2.5ml) Dexamethasone 2mg/5ml Oral Solution twice a day.**
Fourth day:	**500micrograms (1.25ml) Dexamethasone 2mg/5ml Oral Solution twice a day.**
Fifth day:	**500micrograms (1.25ml) Dexamethasone 2mg/5ml Oral Solution twice a day.**

Sixth day:	500micrograms (1.25ml) Dexamethasone 2mg/5ml Oral Solution.
Seventh day:	500micrograms (1.25ml) Dexamethasone 2mg/5ml Oral Solution.
Eighth day:	Re-assessment.

This schedule is designed to ensure adequate therapy during acute episodes whilst minimizing the risk of over dosage 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 2mg/5ml 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 2mg/5ml 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 2mg/5ml 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.

Paediatric population:

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

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.

Method of administration

For Oral use.

4.3 Contradindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

- 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 provide details of prescriber, drug, dosage and the duration of treatment.

An adrenocortical insufficiency, which is caused by glucocorticoid treatment, can, depending on the dose and length of treatment, remain for many months, and in some cases more than a year, after discontinuation of treatment. During treatment with Dexamethasone 2mg/5ml Oral Solution for specific physical stress conditions (trauma, surgery, childbirth, etc.), a temporary increase in dose may be required. Because of the possible risk in stressful conditions, a corticosteroid ID should be made for patients undergoing long-term treatment. Even in cases of prolonged adrenocortical insufficiency after discontinuation of treatment, the administration of glucocorticoids can be necessary in physically stressful situations. An acute therapy-induced adrenocortical insufficiency can be minimized by slow dose reduction until a planned discontinuation time. Treatment with Dexamethasone 2mg/5ml Oral Solution should only be implemented in the event of the strongest indications and, if necessary, additional targeted anti-infective treatment administered for the following illnesses:

- Acute viral infections (Herpes zoster, Herpes simplex, Varicella, herpetic keratitis)

- HBsAG-positive chronic active Hepatitis

- Approx. 8 weeks prior through 2 weeks after vaccinations with live vaccines

- Systemic mycoses and parasitosis (e.g. Nematodes)

- Poliomyelitis

- Lymphadenitis after BCG vaccination

- Acute and chronic bacterial infections

- With a history of tuberculosis (reactivation risk) Use only under tuberculostatic protection

In addition, treatment with Dexamethasone 2mg/5ml Oral Solution should only be implemented under strong indications and, if necessary, additional specific treatment must be implemented for:

- Gastrointestinal ulcers

- Severe osteoporosis

- Difficult to regulate high blood pressure

- Difficult to regulate Diabetes mellitus

- Psychiatric disorders (including history)

- Angle closure glaucoma and wide-angle glaucoma

- Corneal ulcerations and corneal injuries

Because of the risk of an intestinal perforation, Dexamethasone 2mg/5ml Oral Solution must only be used under urgent indication and under appropriate monitoring for:

- Severe ulcerative colitis with threatened perforation

- Diverticulitis

- Entero-anastomosis (immediately postoperative)

Signs of peritoneal irritation after gastrointestinal perforation may be absent in patients receiving high doses of glucocorticoids. A higher need for insulin, or oral antidiabetics, must be taken into consideration when administering Dexamethasone 2mg/5ml Oral Solution to diabetics. Regular blood pressure monitoring is necessary during treatment with Dexamethasone 2mg/5ml Oral Solution, particularly during administration of higher doses and with patients with difficult to regulate high blood pressure. Because of the risk of deterioration, patients with severe cardiac insufficiency should be carefully monitored. Treatment with Dexamethasone 2mg/5ml Oral Solution can conceal the symptoms of an existing or developing infection thereby making a diagnosis more difficult.

The prolonged use of even small amounts of Dexamethasone leads to an increased risk of infection, even by microorganisms which otherwise rarely cause infections (so-called opportunistic infections). Vaccinations with inactivated vaccine are always possible. However, it should be noted that the immune reaction and thereby the success of inoculation, can be affected by higher doses of corticoids.

Regular checkups with doctors (including vision checkups in three-month intervals) are advised during long-term treatment with Dexamethasone 2mg/5ml Oral Solution.

At high doses, sufficient calcium intake and sodium restriction, as well as serum potassium levels should be monitored. Depending on the length and dosage of the treatment, a negative influence on calcium metabolism can be expected, so that an osteoporosis prophylaxis is recommended. This applies, above all, to co-existing risk factors like familial disposition, increased age, after menopause, insufficient protein and calcium intake, heavy smoking, excessive alcohol intake, as well as insufficient exercise. Prevention consists of sufficient calcium and vitamin D intake and physical activity. Additional medical treatment should be considered in the event of pre-existing osteoporosis. The following risks should be considered upon interruption or discontinuation of long-term glucocorticoid administration:

- Exacerbation or recurrence of the underlying disease, acute adrenal insufficiency, corticosteroid withdrawal syndrome.

- Certain viral diseases (chickenpox, measles) in patients treated with glucocorticoids, may be very severe.

- Children and immunocompromised persons without previous chickenpox or measles infection are particularly at risk. If these people have contact with people infected with measles or chickenpox while undergoing treatment with Dexamethasone 2mg/5ml Oral Solution, a preventative treatment should be introduced 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.

Tumour lysis syndrome

In post marketing experience tumour lysis syndrome (TLS) has been reported in patients with haematological malignancies following the use of dexamethasone alone or in combination with other chemotherapeutic agents. Patient at high risk of TLS, such as patients with high proliferative rate, high tumour burden, and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precaution taken.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Preterm neonates

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

Paediatric population

Corticosteroids cause a dose-dependent inhibition of growth in infancy, childhood, and adolescence, which may be irreversible. Therefore, during long-term treatment with Dexamethasone 2mg/5ml Oral Solution, the indication should be very strongly presented in children and their growth rate should be checked regularly.

Use in the elderly

The adverse effects of systemic corticosteroids can have serious consequences especially in old age, mainly osteoporosis, hypertension, hypokalemia, diabetes, susceptibility to infection and skin atrophy. Close clinical monitoring is required to prevent life-threatening reactions.

Influence of diagnostic tests

Glucocorticoids can suppress skin reaction to allergy testing. They can also affect the nitroblue tetrazolium test for bacterial infections and cause false-negative results.

Note on doping

The use of doping tests when taking Dexamethasone 2mg/5ml Oral Solution can lead to positive results.

Excipient Warnings

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Dexamethasone 2mg/5ml Oral Solution contains these kinds of sugar:

• 0.14 g sorbitol in each ml. When taken according to the dosage recommendations each dose supplies up to 3.15 g of sorbitol.

• 0.275 g maltitol in each ml. When taken according to the dosage recommendations each dose supplies up to 6.2 g of maltitol.

Dexamethasone 2mg/5ml Oral Solution contains 0.09 g propylene glycol in each ml. When taken according to the dosage recommendations each dose supplies up to 2 g of propylene glycol

4.5 Interaction with other drug 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, ephedrine, rifabutin, carbamazepine and rifampicin may lead to decreased plasma concentrations of dexamethasone and the dose may need to be increased. Concomitant administration of inhibitors of CYP3A4 such as ketoconazole, ritonavir and erythromycin may lead to increased plasma concentrations of dexamethasone.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

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 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 NSAIDs 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 hypoprothrombinemia.

Antitubercular drugs: Serum concentrations of isoniazid may be decreased.

Ciclosporin: Increased activity of both ciclosporin 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 nitroblue tetrazolium test for bacterial infection and produce false-negative results.

Vaccines attenuated live

Risk of fatal systemic disease

Praziquantel:

Decrease in praziquantel plasma 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 Fertility, pregnancy and lactation

Pregnancy

Dexamethasone crosses the placenta. Administration of corticosteroids to pregnant animals can cause abnormalities in 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 Section 5.3). Long-term or repeated corticosteroid therapy in pregnancy increases the risk of intrauterine growth retardation. In newborns exposed to corticosteroids in the prenatal period, there is an increased risk of adrenal insufficiency, which under normal circumstances undergoes spontaneous postnatal regression, and is rarely of clinical significance. Dexamethasone should be prescribed during pregnancy, and particularly in the first trimester, only if the benefit outweighs the risks for the mother and child.

Breast-feeding

Glucocorticoids are excreted in breast milk. There are no known risks to infants. Nevertheless, extra caution should be exercised regarding its indication during pregnancy. Should the relevant condition require higher doses, treatment should be discontinued.

4.7 Effects on ability to drive and use machines

Dexamethasone 0.5mg/5ml Oral Solution has no or negligible influence on the ability to drive and use machines.

So far, there is no evidence that Dexamethasone 0.5mg/5ml Oral Solution affects the ability to drive or operate machinery.

4.8 Undesirable effects

The incidence of anticipated adverse effects, such as the suppression of the hypothalamic-pituitary-adrenal axis correlates with the relative potency of the substance, dose, time of day of administration and duration of treatment. During a short-term therapy, in compliance with the dosage recommendations and close monitoring of patients, the risk of side effects is low. The side effects below have been reported with the following frequency:

Not known (cannot be estimated from the available data)

System organ class	Frequency	Undesirable effects
Infections and infestations	Not known	Increased susceptibility to, or exacerbation of, (latent) infections with masking of clinical symptoms, opportunistic infections, reactivation of latent tuberculosis, exacerbation of eye infections, candidiasis
Blood and lymphatic system disorders	Not known	Leukocytosis, lymphopenia, eosinopenia, polycythemia
Immune system disorders	Not known	Hypersensitivity reactions including anaphylaxis, immunosuppression (see also under "Infections and parasitic diseases")
Endocrine disorders	Not known	Suppression of the hypothalamic-pituitary-adrenal axis and induction of Cushing's syndrome (typical symptoms: full-moon face, plethora, truncal obesity), secondary adrenal and pituitary insufficiency (especially in stress such as trauma or surgery)
Metabolism and nutrition disorders	Not known	Weight gain, negative protein and calcium balance, increased appetite, sodium and water retention, potassium loss (caution: rhythm disorders), hypokalemic alkalosis, manifestation of latent diabetes mellitus, impaired carbohydrate tolerance with increased dose requirements of antidiabetic therapy, hypercholesterolemia, hypertriglyceridemia
Psychiatric disorders	Not known	Psychological dependence, depression, insomnia, aggravated schizophrenia, mental illness, from euphoria to manifest psychosis
Nervous system disorders	Not known	Increased intracranial pressure with papilloedema in children (pseudotumor cerebri) usually following discontinuation of treatment; manifestation of latent epilepsy, increased seizures in overt epilepsy

Eye disorders	Not known	Elevated intraocular pressure, glaucoma, papilloedema, cataract, mainly with posterior subcapsular opacity, corneal and scleral atrophy, increased ophthalmic viral, fungal and bacterial infections, worsening of symptoms associated with corneal ulcers, Chorioretinopathy, Vision, blurred (see also section 4.4)
Cardiac disorders	Not known	Cardiac muscle rupture after recent history of myocardial infarction, congestive heart failure in predisposed patients
Vascular disorders	Not known	Hypertension, vasculitis, increased atherosclerosis and risk of thrombosis/thromboembolism
Respiratory, thoracic and mediastinal disorders	Not known	Hiccough
Gastrointestinal disorders	Not known	Dyspepsia, gastric ulcers with perforation and bleeding, acute pancreatitis, ulcerative esophagitis, flatulence, nausea, vomiting
Skin and subcutaneous disorders	Not known	Hirsutism, hypertrichosis, skin atrophy, telangiectasia, striae, erythema, steroid acne, petechiae, ecchymosis, allergic dermatitis, urticaria, angioneurotic oedema, thinning hair, pigment disorders, increased capillary fragility, perioral dermatitis
Musculoskeletal and connective tissue disorders	Not known	Growth inhibition in infants, children and adolescents, premature epiphyseal closure, osteoporosis, fractures of the spine and long bones, aseptic necrosis of the femoral and the humeral bones, tendon tears, proximal myopathy, muscle weakness, loss of muscle mass
Reproductive system and breast disorders	Not known	Irregular menses, amenorrhea, impotence
General disorders and administration site conditions	Not known	Delayed wound healing, discomfort, steroid withdrawal syndrome: a too rapid reduction in corticosteroid dose after prolonged treatment can lead to acute adrenal insufficiency, hypotension, and death. A withdrawal syndrome may present with fever, myalgia, arthralgia, rhinitis, conjunctivitis, pain, itchy skin nodules and weight loss.
Injury, poisoning and procedural complications	Not known	Reduced response to vaccination and skin tests, tendency to bruise

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 to the regulatory bodies such as NAFDAC.

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

Pharmacotherapeutic Group: Glucocorticoids

ATC Code: H02A B02

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.

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. In healthy subjects a plasma half life of 3-6 hours has been observed however in studies of patients this can be reduced to under 2 hours. 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, intra-uterine growth can be delayed. All these effects were seen at high dosages.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

S/N	Raw Materials	Specification
1.	Sodium CMC	B.P
5.	Methyl paraben	B.P
6.	Propyl paraben	B.P
7.	Glycerine	B.P
8.	Sugar	B.P
9.	Strawberry flavour	B.P
10.	Camoisine red	B.P

11.	Sodium benzoate	B.P
12	Xanthan gum	BP
13	Tween 80	BP
14	Treated water	B.P

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

After first opening: 3 months

6.4 Special precautions for storage

Do not store above 30°C.

Do not refrigerate.

The storage at temperatures higher than 30°C could lead to precipitation inside the solution. Do not use the product if solid particles are observed inside the solution.

6.5 Nature and contents of container

Amber (Type III) glass bottle, with child-resistant, tamper-evident screw cap.

Capacity: 100 ml

6.6 Special precautions for disposal of used medicinal product or waste materials derived from such medicinal product and other handling of the product

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

NAME:
NALIS PHARMACEUTICALS LTD

ADDRESS:

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8. DRUG PRODUCT MANUFACTURER

NAME:
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9. NAFDAC REGISTRATION NUMBER(S):

A11-100040