For PPB use only

1.17 **Summary Product Characteristics (SPC)**

1.17.1 Product Information for Health Professional:

1.1 Product Name: DYNACORT ORAL SUSPENSION

1.2 Strength: 6 MG / 5 ML

Pharmaceutical Dosage Form : Powder , Solid Dosage form

2.0 Quality and Quantitative Composition :

2.1 Quality Declaration:

Each 5 ml Suspension
(After Reconstitution) Contains:
Deflazacort 6 mg
Flavoured Base

2.2 Quantitative Declaration :

INGREDIENTS	**MG/ Bottle**
Deflazacort $	36.0
Pharmagrade Sugar (30/80 mesh) #	8778
Sucralose BP	20.0
Avicel CL611 USPNF*	550
Xanthangum BP	10.0
Colloidal Silicon Dioxide BP	350
Citric Acid Anhydrous	20.0
Methyl Hydroxy Benzoate BP	10.0
Propyl Hydroxy Benzoate BP	1.00
Flavour Strawberry	155
Flavour Peppermint	70.0

3.0 Pharmaceutical Dosage Form :

Powder, Solid Dosage form

4.0 Clinical Particulars :

4.1 Therapeutic Indications :

A wide range of conditions may sometimes need treatment with glucocorticoids. The indications include:

- Anaphylaxis, asthma, severe hypersensitivity reactions
- Rheumatoid arthritis, juvenile chronic arthritis, polymyalgia rheumatica

- Systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease (other than systemic sclerosis), polyarteritis nodosa, sarcoidosis
- Pemphigus, bullous pemphigoid, pyoderma gangrenosum Minimal change nephrotic syndrome, acute interstitial nephritis
- Rheumatic carditis
- Ulcerative colitis, Crohn's disease
- Uveitis, optic neuritis
- Autoimmune haemolytic anaemia, idiopathic thrombocytopenic purpura
- Acute and lymphatic leukaemia, malignant lymphoma, multiple myeloma
- Immune suppression in transplantation

4.2 Posology and method of administration

Deflazacort is a glucocorticoid derived from prednisolone and 6mg of deflazacort has approximately the same anti-inflammatory potency as 5mg prednisolone or prednisone.

Doses vary widely in different diseases and different patients. In more serious and life-threatening conditions, high doses of deflazacort may need to be given. When deflazacort is used long term in relatively benign chronic diseases, the maintenance dose should be kept as low as possible. Dosage may need to be increased during periods of stress or in exacerbation of illness.

The dosage should be individually titrated according to diagnosis, severity of disease and patient response and tolerance. The lowest dose that will produce an acceptable response should be used (see Warnings and Precautions).

Adults

For acute disorders, up to 120 mg/day deflazacort may need to be given initially. Maintenance doses in most conditions are within the range 3 - 18 mg/day. The following regimens are for guidance only.

Rheumatoid arthritis: The maintenance dose is usually within the range 3 - 18 mg/day. The smallest effective dose should be used and increased if necessary.

Bronchial asthma: In the treatment of an acute attack, high doses of 48-72 mg/day may be needed depending on severity and gradually reduced once the attack has been controlled. For maintenance in chronic asthma, doses should be titrated to the lowest dose that controls symptoms.

Other conditions: The dose of deflazacort depends on clinical need titrated to the lowest effective dose for maintenance. Starting doses may be estimated on the basis of ratio of

	5mg prednisone or prednisolone to 6mg deflazacort.

	Hepatic Impairment In patients with hepatic impairment, blood levels of deflazacort may be increased. Therefore the dose of deflazacort should be carefully monitored and adjusted to the minimum effective dose. **Renal Impairment** In renally impaired patients, no special precautions other than those usually adopted in patients receiving glucocorticoid therapy are necessary. **Elderly** In elderly patients, no special precautions other than those usually adopted in patients receiving glucocorticoid therapy are necessary. The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age (see Warnings and Precautions). **Children** There has been limited exposure of children to deflazacort in clinical trials. In children, the indications for glucocorticoids are the same as for adults, but it is important that the lowest effective dosage is used. Alternate day administration may be appropriate (see Warnings and Precautions). Doses of deflazacort usually lie in the range 0.25 - 1.5 mg/kg/day. The following ranges provide general guidance: ***Juvenile chronic arthritis:*** The usual maintenance dose is between 0.25 - 1.0 mg/kg/day. ***Nephrotic syndrome:*** Initial dose of usually 1.5 mg/kg/day followed by down titration according to clinical need. ***Bronchial asthma:*** On the basis of the potency ratio, the initial dose should be between 0.25 - 1.0 mg/kg deflazacort on alternate days. **Deflazacort withdrawal** In patients who have received more than physiological doses of systemic corticosteroids (approximately 9mg per day or equivalent) 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 equivalent to 9mg deflazacort 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 up to 48 mg daily of deflazacort, or equivalent 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 48 mg daily of deflazacort (or equivalent),

• Patients repeatedly taking doses in the evening.

4.3 Contraindications

Systemic infection unless specific anti-infective therapy is employed.

Hypersensitivity to deflazacort or any of the ingredients. Patients receiving live virus immunisation.

4.4 Special Warnings and precaution for use

A patient information leaflet should be supplied with this product.

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

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 alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity.

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 which could be fatal, being tapered off over weeks or months according to the dose and duration of treatment. During prolonged therapy, any intercurrent illness, trauma 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 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.

Anti-inflammatory/immunosuppressive effects and infection

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

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 chicken pox 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 immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 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.

Patients should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.

Live vaccines should not be given to individuals with impaired responsiveness. The antibody response to other vaccines may be diminished.

Systemic glucocorticoid treatment can cause chorioretinopathy which can lead to visual disorders including visual loss. Prolonged use of systemic glucocorticoid treatment even at low dose can cause chorioretinopathy (see section 4.8).

Prolonged use of glucocorticoids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Use in active tuberculosis should be restricted to those cases of fulminating and disseminated tuberculosis in which deflazacort is used for management with appropriate antituberculosis regimen. If glucocorticoids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged glucocorticoid therapy, these patients should receive chemoprophylaxis.

Tendonitis and tendon rupture are known class effect of glucocorticoids. The risk of such reactions may be increased by coadministration of quinolones (see section 4.8).

Special precautions

The following clinical conditions require special caution and frequent patient monitoring is necessary:-

• Cardiac disease or congestive heart failure (except in the presence of active rheumatic carditis), hypertension, thromboembolic disorders. Glucocorticoids can cause salt and water retention and increased excretion of potassium. Dietary salt restriction and potassium supplementation may be necessary.

• Gastritis or oesophagitis, diverticulitis, ulcerative colitis if there is probability of impending perforation, abscess or pyogenic infections, fresh intestinal anastomosis, active or latent peptic ulcer.

• Diabetes mellitus or a family history, osteoporosis, myasthenia gravis, renal insufficiency.

• Emotional instability or psychotic tendency, epilepsy.

• Previous corticosteroid-induced myopathy.

• Liver failure.

• Hypothyroidism and cirrhosis, which may increase glucocorticoid effect.

• Ocular herpes simplex because of possible corneal perforation.

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. Glucocorticoids are known to cause irregular menstruation and leukocytosis, care should be taken with deflazacort. **Paediatric population** Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence which may be irreversible. **Use in 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. Since complications of glucocorticoid therapy are dependent on dose and duration of therapy, the lowest possible dose must be given and a risk/benefit decision must be made as to whether intermittent therapy should be used. **4.5 Interaction with other medicinal products and other forms of interactions** The same precautions should be exercised as for other glucocorticoids. Deflazacort is metabolised in the liver. It is recommended to increase the maintenance dose of deflazacort if drugs which are liver enzyme inducers are co-administered, e.g.

	rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and

	aminoglutethimide. For drugs which inhibit liver enzymes, e.g. ketoconazole it may be possible to reduce the maintenance dose of deflazacort. In patients taking estrogens, corticosteroid requirements may be reduced. The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, beta 2-agonists, xanthines and carbenoxolone are enhanced. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding. In patients treated with systemic corticosteroids, use of non-depolarising muscle relaxants can result in prolonged relaxation and acute myopathy. Risk factors for this include prolonged and high dose corticosteroid treatment, and prolonged duration of muscle paralysis. This interaction is more likely following prolonged ventilation (such as in the ITU setting). The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. As glucocorticoids can suppress the normal responses of the body to attack by micro-organisms, it is important to ensure that any anti-infective therapy is effective and it is recommended to monitor patients closely. Concurrent use of glucocorticoids and oral contraceptives should be closely monitored as plasma levels of glucocorticoids may be increased. This effect may be due to a change in metabolism or binding to serum proteins. Antacids may reduce bioavailability; leave at least 2 hours between administration of deflazacort and antacids. 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.

4.6 Pregnancy and Lactation

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs, however, deflazacort does cross the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine 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. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

Lactation

Corticosteroids are excreted in breast milk, although no data are available for deflazacort. Doses of up to 50 mg daily of deflazacort are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression but the benefits of breast feeding are likely to outweigh any theoretical risk.

4.7 Effects on ability to drive and use machine :

On the basis of the pharmacodynamic profile and reported adverse events, it is unlikely that deflazacort will produce an effect on the ability to drive and use machines.

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 (see section 4.4).

The following CIOMS frequency rating is used: Very common (≥1/10); common

	(≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10 000 to <1/1000); very rare (<1/10 000), not known (cannot be estimated from the available data).

	Endocrine disorders Uncommon: Suppression of the hypothalamic-pituitary-adrenal axis, amenorrhoea, Cushingoid facies. Not known: Growth suppression in infancy, childhood and adolescence. **Metabolism and nutrition disorders** Common: Weight gain. Uncommon: impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy, sodium and water retention with hypertension, potassium loss and hypokalaemic alkalosis when coadministered with beta 2-agonist and xanthines. Not known: Negative protein and calcium balance, increased appetite. **Infections and Infestations** Uncommon: Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see section 4.4). Not known: candidiasis. **Musculoskeletal and connective tissue disorders** Uncommon: Osteoporosis, vertebral and long bone fractures. Rare: Muscle wasting Not known: avascular osteonecrosis, tendonitis and tendon rupture when coadministered with quinolones (see section 4.4), myopathy (acute myopathy may be precipitated by non-depolarising muscle relaxants – see section 4.5), negative nitrogen balance. **Reproductive system and breast disorders** Not known: Menstrual irregularity **Cardiac disorders** Not known: Heart failure **Nervous system disorders** Uncommon: Headache, vertigo. Not known: restlessness, Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal, aggravation of epilepsy. **Psychiatric disorders** A wide range of psychiatric reactions including affective disorders such as:

	Uncommon: depressed and labile mood. Not known: irritable, euphoric, suicidal thoughts.

	Psychotic reactions including: Not known: mania, delusions, hallucinations, aggravation of schizophrenia Other reactions including: Uncommon: behavioural disturbances Not known: 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. **Eye disorders** Not known: Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts especially in children, chorioretinopathy (see section 4.4), corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases. **Gastrointestinal disorders** Uncommon: Dyspepsia, peptic ulceration, haemorrhage, nausea. Not known: perforation of peptic ulcer, acute pancreatitis (especially in children), candidiasis. **Skin and subcutaneous tissue disorders** Uncommon: hirsutism, striae, acne, Rare: bruising Not known: Skin atrophy, telangiectasia. **General disorders and administration site conditions** Uncommon: Oedema. Not known: impaired healing. **Immune system disorders** Uncommon: Hypersensitivity including anaphylaxis has been reported. **Blood and lymphatic system disorders** Not known: Leukocytosis **Vascular disorders** Not known: Thromboembolism in particular in patients with underlying conditions associated with increased thrombotic tendency, rare incidence of benign intracranial

	hypertension

Withdrawal symptoms and signs

Not known: Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4).

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight. This may occur in patients even without evidence of adrenal insufficiency.

4.9 Overdose

It is unlikely that treatment is needed in cases of acute overdosage. The LD50 for the oral dose is greater than 4000 mg/kg in laboratory animals.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Deflazacort is a glucocorticoid. Its anti-inflammatory and immunosuppressive effects are used in treating a variety of diseases and are comparable to other anti-inflammatory steroids. Clinical studies have indicated that the average potency ratio of deflazacort to prednisolone is 0.69-0.89.

5.2 Pharmacokinetic Properties

Orally administered deflazacort appears to be well absorbed and is immediately converted by plasma esterases to the pharmacologically active metabolite (D 21-OH) which achieves peak plasma concentrations in 1.5 to 2 hours. It is 40% protein-bound and has no affinity for corticosteroid-binding-globulin (transcortin). Its elimination plasma half-life is 1.1 to 1.9 hours. Elimination takes place primarily through the kidneys; 70% of the administered dose is excreted in the urine. The remaining 30% is eliminated in the faeces. Metabolism of D 21-OH is extensive; only 18% of urinary excretion represents D 21-OH. The metabolite of D 21-OH, deflazacort 6-beta-OH, represents one third of the urinary elimination.

5.3 Preclinical safety data

	Safety studies have been carried out in the rat, dog, mouse and monkey. The findings are consistent with other glucocorticoids at comparable doses. Teratogenic effects

	demonstrated in rodents and rabbits are typical of those caused by other glucocorticoids. Deflazacort was not found to be carcinogenic in the mouse, but studies in the rat produced carcinogenic findings consistent with the findings with other glucocorticoids. **6. Pharmaceutical Particulars** **6.1 List of Excipients** • Pharmagrade Sugar (30/80 mesh) • Sucralose BP • Avicel CL611 USPNF • Xanthangum BP • Colloidal Silicon Dioxide BP • Citric Acid Anhydrous • Methyl Hydroxy Benzoate BP • Propyl Hydroxy Benzoate BP • Flavour Strawberry • Flavour Peppermint **6.2 Incompatibilities:** Not Applicable **6.3 Shelf Life:** 36 Months **6.4 Special precautions for Storage:** Store in a cool dry place below 30°C. Keep medicines out of reach of children. **6.5 Nature and Contents of container** 30ml Amber coloured glass bottle & each bottle is packed in carton with pack insert & measuring spoon

	7. Marketing Authorization Holder **Name: Galaxy Pharmaceutical Ltd** Address: 1st Doctor's Park, 3rd Parklands, P.O. Box 39107- 00623, Nairobi- Kenya Country: Kenya Telephone:020-3748551/2/3/4 Telefax:3740766 E-Mail: info@galaxypharma.co.ke **8. Manufacturer** Factory : Skybiotech Life Sciences Pvt. Ltd. Address: Gut No. 5, Gevrai Tanda, Paithan Road, Aurangabad (M.S) India. Country : India Telephone: (91) (240) 2694545 Telefax : (91) (240) 2694488 Email : aher.sr@yahoo.com
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