BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of drug product

DORCO-DEXA

1.1 (Trade) name of product

DEXAMETHASONE TABLETS B.P. 0.5 MG

1.2 Strength

Each uncoated tablet contains:

Dexamethasone BP…….0.5 mg

Excipients……Q.S.

1.3 Pharmaceutical Dosage Form

Uncoated tablet

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

2. Qualitative & Quantitative Composition

2.1 Qualitative Declaration

Each uncoated tablet contains:

Dexamethasone BP…….0.5 mg

Excipients……Q.S.

2.2 Quantitative Declaration

Batch Formula:

Batch Size: 40,84,320 tablets

Sr. No.	Ingredients	Specifications	Reason For Inclusion	Label Claim	Overages (%)	Quantity/ Unit (mg)	Quantity/ Batch (kg)
1.	Dexamethasone	BP	Active	0.5 mg	----	0.500	2.043
2.	Dibasic Calcium Phosphate	BP	Glidant	----	----	53.325	217.796
3.	Starch	BP	Binder	----	----	70.125	286.412
4.	Calcium carbonate	BP	Diluent	----	----	33.331	136.135
5.	gelatin	BP	Binder	----	----	1.000	4.085
6.	Sodium Methyl paraben	BP	Preservative	----	----	0.125	0.510
7.	Sodium propyl paraben	BP	Preservative	----	----	0.094	0.384
8.	Starch	BP	Diluent	----	----	4.000	16.338
9.	Magnesium Stearate	BP	Lubricant	----	----	3.749	15.316
10.	Talcum	BP	Lubricant	----	----	3.749	15.316

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

3. Pharmaceutical Dosage Form

Uncoated tablet

4. Clinical particulars

4.1 Therapeutic indications

Indicated in a wide variety of disorders amenable to glucocorticoid therapy, as well as an adjunct in the control of cerebral oedema.

4.2 Posology and method of administration

Posology

In general, glucocorticoid dosage depends on the severity of the condition and response of the patient. Under certain circumstances, for instance in stress and changed clinical picture, extra dosage adjustments may be necessary. If no favourable response is noted within a couple of days, glucocorticoid therapy should be discontinued.

Adults

Usually, daily oral dosages of 0.5 - 10 mg are sufficient. In some patients higher dosages may be temporarily required to control the disease. Once the disease is under control the dosage should be reduced or tapered off to the lowest suitable level under continuous monitoring and observation of the patient. **(See Section 4.4)**

For a short dexamethasone suppression test, 1mg dexamethasone is given at 11 p.m. and plasma cortisol measured the next morning. Patients who do not show a decrease in cortisol can be exposed to a longer test: 500 micrograms dexamethasone is given at 6 hourly intervals for 48 hours followed by 2mg every 6 hours for a further 48 hours. 24 hour-urine collections are made before, during and at the end of the test for determination of 17-hydroxycorticosteroids.

Paediatric population

0.01-0.1mg/kg of body weight daily.

Dosage of glucocorticoids should be adjusted on the basis of the individual patient's response.

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

4.3 Contraindications

Systemic infection unless specific anti-infective therapy is employed.

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

Avoid live vaccines in patients receiving immunosuppressive doses (serum antibody response diminished).

In general no contraindications apply in conditions where the use of glucocorticoids may be lifesaving.

4.4 Special warnings and precautions for use

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. Patients 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.

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 for 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.

The results of a randomised, placebo-controlled study suggest an increase in mortality if methylprednisolone therapy starts more than two weeks after the onset of Acute Respiratory Distress

Syndrome (ARDS). Therefore, treatment of ARDS with corticosteroids should be initiated within the first two weeks of onset of ARDS (see also section 4.2.).

Preterm neonates:

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

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.

Dexamethasone withdrawal

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 1mg 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 corticosteroid 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 6mg 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:

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

• 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 6mg daily of dexamethasone.

• Patients repeatedly taking doses in the evening.

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.

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

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 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.

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

MeaslesPatients 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.

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.

Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary

a. Osteoporosis (post-menopausal females are particularly at risk)

b. Hypertension or congestive heart failure

c. Existing or previous history of severe affective disorders (especially previous steroid psychosis)

d. Diabetes mellitus (or a family history of diabetes)

e. History of tuberculosis

f. Glaucoma (or a family history of glaucoma)

g. Previous corticosteroid-induced myopathy

h. Liver failure

i. Renal insufficiency

j. Hypothyroidism

k. Epilepsy

l. Peptic ulceration

m. Migraine

n. Certain parasitic infestations in particular amoebiasis

o. Incomplete natural growth since glucocorticoids on prolonged administration may accelerate epiphyseal closure

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

Caution should be exercised when using corticosteroids in patients who have recently suffered myocardial infarction as myocardial rupture has been reported.

After administration of glucocorticoids serious anaphylactoid reactions such as glottis oedema, urticaria and bronchospasm have occasionally occurred particularly in patients with a history of allergy.

If such an 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.

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

Paediatric population

Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible.

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.

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

4.5 Interaction with other medicinal products and other forms of interaction

Rifampicin, rifabutin, carbamazepine, phenobartital, phenytoin, primidone, and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced.

Dexamethasone is a moderate inducer of CYP 3A4. Co-administration of dexamethasone with other drugs that are metabolized by CYP 3A4 (e.g., indinavir, erythromycin) may increase their clearance, resulting in decreased plasma concentrations.

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.

Ephedrine also accelerates the metabolism of dexamethasone.

The effects of anticholinesterases are antagonised by corticosteroids in myasthenia gravis.

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 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.

Oral contraceptives (oestrogens and progestogens) increase plasma concentration of corticosteroids.

The antiviral drug ritonavir also increases the plasma concentration of dexamethasone.

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

The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

Patients taking NSAIDs should be monitored since the incidence and/or severity of gastro-intestinal ulceration may increase.

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

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

Antacids, especially those containing magnesium trisilicate have been reported to impair the gastrointestinal absorption of glucocorticoid steroids. Therefore, doses of one agent should be spaced as far as possible from the other.

MODULE -1 ADMINISTRATIVE INFORMATION

4.6 Fertility, pregnancy and lactation

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs, however, dexamethasone readily crosses 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 (see also section 5.3). 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.

Breastfeeding

Corticosteroids may pass into breast milk, although no data are available for dexamethasone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

4.7 Effects on ability to drive and use machines

Not Known.

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).

Endocrine/metabolic

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

Suppression of the hypothalamic-pituitary-adrenal axis, growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea, Cushiongoid faces, hirsutism, weight gain, premature epiphyseal closure, impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy, negative protein and calcium balance, increased appetite

Anti-inflammatory and Immunosuppressive effects

Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see section 4.4), decreased responsiveness to vaccination and skin tests

Musculoskeletal

Osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, proximal myopathy

Fluid and electrolyte disturbance

Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis

Neuropsychiatric

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.

Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal. Aggravation of epilepsy. Psychological dependence.

Ophthalmic

Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of opthalmic viral or fungal diseases, chorioretinopathy

Eye disorders

Vision, blurred (see also section 4.4)

Gastrointestinal

Dyspepsia, peptic ulceration with perforation and haemorrhage, acute pancreatitis, oesophagael ulceration and candidiasis, abdominal distension and vomiting

Dermatological

Impaired healing, skin atrophy, bruising, telangiectasia, striae, acne

General

Hypersensitivity, including anaphylaxis and angioedema, have been reported. Leucocytosis, thromboembolism, myocardial rupture following recent myocardial infarction, nausea, malaise, hiccups

Withdrawal symptoms and signs

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.

4.9 Overdose

It is difficult to define an excessive dose of a corticosteroid as the therapeutic dose will vary according to indication and patient requirements. Exaggeration of corticosteroid related adverse effects may occur. Treatment should be asymptomatic and supportive as necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use, Glucocorticoids,

ATC code: H02AB02

Dexamethasone is a synthetic glucocorticoid whose anti-inflammatory potency is 7 times greater than prednisolone. Like other glucocorticoids, dexamethasone also has anti-allergic, antipyretic and immunosuppressive properties.

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

Dexamethasone has practically no water and salt-retaining properties, and is therefore particularly suitable for use in patients with cardiac failure or hypertension. Because of its long biological half-life (36-54 hours), dexamethasone is especially suitable in conditions where continuous glucocorticoid action is desired.

5.2 Pharmacokinetic properties

Absorption

Corticosteroids, are, in general, readily absorbed from the gastro-intestinal tract. They are also well absorbed from sites of local application. Water-soluble forms of corticosteroids are given by intravenous injection for a rapid response; more prolonged effects are achieved using lipid-soluble forms of corticosteroids by intramuscular injection.

Distribution

Corticosteroids are rapidly distributed to all body tissues. They cross the placenta and may be excreted in small amounts in breast milk.

Most corticosteroids in the circulation are extensively bound to plasma proteins, mainly to globulin and less so to albumin. The corticosteroid-binding globulin has high affinity but low binding capacity, while the albumin has low affinity but large binding capacity. The synthetic corticosteroids are less extensively protein bound than hydrocortisone (cortisol). They also tend to have longer half-lives.

Biotransformation and Elimination

Corticosteroids are metabolised mainly in the liver but also in the kidney, and are excreted in the urine. The slower metabolism of the synthetic corticosteroids with their lower protein-binding affinity may account for their increased potency compared with the natural corticosteroids.

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.

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

6. Pharmaceutical particulars

6.1 List of excipients

Dibasic Calcium Phosphate

Starch

Calcium carbonate

gelatin

Sodium Methyl paraben

Sodium propyl paraben

Starch

Magnesium Stearate

Talcum

6.2 Incompatibilities

Not Applicable.

6.3 Shelf Life

36 Months

6.3 Special Precautions for Storage

Store below 30°C. Protect from light.

6.4 Nature and Contents of Container

10 tablets pack in ALU/PVC Blister. Such a 10 Blister packed in a monocarton along with package insert.

BRAND NAME:	**DORCO-DEXA**
GENERIC NAME:	**DEXAMETHASONE TABLETS B.P. 0.5 MG**

MODULE -1 ADMINISTRATIVE INFORMATION

7. Marketing authorisation holder

JSP PHARMA CO. (NIG) LTD

NO. 69 BALLAT HUGHES ROAD,

SABON GARI, KANO, NIGERIA.

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text