Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Cortimax 6 mg Tablets
Cortimax 12 mg Tablets

2. Qualitative and quantitative composition

Cortimax 6 mg Tablets
Each uncoated tablet contains Deflazacort 6 mg

Cortimax 12 mg Tablets
Each uncoated tablet contains Deflazacort 12 mg

Excipient(s) with known effect:
Lactose monohydrate
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Uncoated tablet, 6 mg and 12 mg

4. Clinical particulars

4.1 Therapeutic indications

Deflazacort may be used in the treatment of:

- 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 6 mg of deflazacort has approximately the same anti-inflammatory potency as 5 mg prednisolone. Doses vary widely in different indications and different patients. In more serious or life-threatening conditions, high doses of deflazacort may be required. When deflazacort is used long term in relatively benign chronic conditions, the maintenance dose should be kept as low as possible. Dosage may be increased during periods of stress

of exacerbations of the condition. The dosage should be individually titrated according to the diagnosis, severity of disease, patient response and tolerance. The lowest dose that will produce an acceptable response should be used.

Patient Population	**Dosage**
Adults	Up to 120 mg/day deflazacort may be required initially. Maintenance doses in most conditions are within the range of 3-18 mg/day.
Children	There has been limited exposure of children to deflazacort in clinical trials. In children, the indications for glucocorticoid are the same as for adults, but it is important that the lowest effective dosage is used. Alternate day administration may be appropriate. Doses of deflazacort usually lie in the range of 0.25 to 1.5 mg/kg/day.

Condition	**Dosage**
Bronchial asthma	Adult: In the treatment of an acute attack, high doses of 48-72 mg/day may be necessary, depending on severity and gradually reduced once the attack has been controlled. For maintenance in chronic asthma, doses should be tested to the lowest dose that controls the symptoms. Children : On the basis of potency ratio, the initial dose should be between 0.25-1.0 mg/kg/day on alternate days.
Rheumatoid Arthritis	Maintenance dose is usually within the range of 3-18 mg/day. The smallest effective dose should be used and increased if necessary.
Juvenile chronic Arthritis	The usual maintenance dose is between 0.25-1.5 mg/kg/day

<u>Deflazacort withdrawal</u>

In patients who have received more than physiological doses of systemic corticosteroids (approximately 9 mg/ day or equivalent) for >3 weeks, withdrawal should not be abrupt. How the 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 9 mg 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).
- Patents 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 infections unless specific anti-infective therapy is employed
- Hypersensitivity to deflazacort or any of the ingredients listed in the formulation.
- Patients receiving live viral immunization

4.4 Special warnings and precautions for use

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 minimized 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. Corticosteroids should be 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.

When discontinuing long-term administration of corticosteroids, it should be done gradually. The risks associated with sudden discontinuation are exacerbation or recurrence of the underlying disease, adrenocortical insufficiency (which could be fatal) or steroid withdrawal syndrome. Steroid withdrawal syndrome may present with a wide range of signs and symptoms. However, typical symptoms include fever, anorexia, nausea, lethargy, malaise, myalgia, arthralgias, rhinitis, conjunctivitis, desquamation of the skin and painful itchy skin nodules, weakness, hypotension and weight loss. This may occur in patients even without evidence of adrenal insufficiency.

Patients should carry 'Steroid treatment' cards which give clear guidance on the precautions to be taken to minimize 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.

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. 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 recognized. 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 required for exposed nonimmune patents 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 chodoretinopathy which can lead to visual disorders including visual loss. Prolonged use of systemic glucocorticoid treatment even at low dose can cause chorioretinopathy. 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. It 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 effects of glucocorticoids. The risk of such reactions may be increased by coadministration of quinolones.

Renal Impairment
No special precautions other than those usually adopted in patients receiving glucocorticoid therapy are necessary.

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.

Special precautions
The following clinical conditions require special caution and frequent patent monitoring is necessary:

- Cardiac disease or congestive heart failure (except in the presence of active rheumatic carditis), hypertension, thromboembolic disorders. Glucocorticoid 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
- 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 caregivers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids. Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure although dose levels do not allow prediction of the onset, type, severity or duration of reactions.

Most reactions subside after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/caregivers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/caregivers 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.

4.5 Interaction with other medicinal products and other forms of interaction.

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.

Corticosteroids can increase or decrease the effect of anticoagulants (see section 4.4). 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.

Concomitant administration with non-steroidal anti-inflammatory drugs can increase the risk of gastrointestinal ulcers (see section 4.4).

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 ICU 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.

Live attenuated vaccines due to increased risk of generalised potentially fatal vaccine induced disease (see section 4.3 and 4.4). Glucocorticoids may potentiate the replication of germs from live attenuated vaccines.

Antacids may reduce bioavailability; leave at least 2 hours between administration of deflazacort and antacids.

4.6 Pregnancy and Lactation

Pregnancy

When administered for prolonged period or repeatedly during pregnancy, corticosteroids may increase the risk of intrauterine growth retardation. 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.

Pediatric
Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. During prolonged glucocorticoid therapy, these patients should be monitored continuously.

Geriatric Use
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.

4.7 Effects on ability to drive and use machines

The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Vertigo is a possible undesirable effect after treatment with deflazacort. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

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 co-administered 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.
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 co-administered with quinolones, myopathy (acute myopathy may be precipitated by non-depolarising muscle relaxants), negative nitrogen balance.

Reproductive system and breast disorders
Not known: Menstrual irregularity.

Cardiac disorders
Not known: Heart failure, hypertrophic cardiomyopathy in preterm infants

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
Uncommon: depressed and labile mood, behavioural disturbances
Not known: irritable, euphoric, suicidal thoughts, psychotic reactions (including mania, delusions, hallucinations, aggravation of schizophrenia), anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia
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: vision blurred (see section 4.4), 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).

Skin and subcutaneous tissue disorders
Uncommon: hirsutism, striae, acne
Rare: bruising
Not known: severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), 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. 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.

Class effect
Pheochromocytoma crisis has been reported with other systemic corticosteroids and is a known class effect (see section 4.4).

Reporting of suspected adverse reactions
Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS)
https://pv.pharmacyboardkenya.org

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
Pharmacotherapeutic group: corticosteroids for systemic use; Glucocorticoids.
ATC code: H02AB13.

Mechanism of action
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

Absorption

Orally administered deflazacort appears to be well absorbed.

Distribution

The active metabolite D 21-OH achieves peak plasma concentrations in 1.5 – 2 hours. It is 40% protein-bound and has no affinity for corticosteroid-binding-globulin (transcortin).

Biotransformation

Orally administered deflazacort is immediately converted by plasma esterases to the pharmacologically active metabolite (D 21-OH). Metabolism of D 21-OH is extensive. The metabolite of D 21-OH is deflazacort 6-beta-OH.

Elimination

Its elimination plasma half-life is 1.1 – 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

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

Microcrystalline cellulose
Lactose Monohydrate
Sodium Starch Glycolate
Colloidal Silicon Dioxide
Magnesium Stearate

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

24 months

6.4 Special Precautions for storage

Store in a dry place at a temperature not exceeding 25°C.
Keep out of reach of children.

6.5 Nature and Content of container
Cortimax: 1x6T, ALU Strip

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder
ZUVENTUS HEALTHCARE LTD.
Office No.5119,5th floor,'D' Wing,
Oberoi Garden Estates, Chandivali, Andheri (E), Mumbai - 400 072

8. Marketing Authorization Number
Cortimax 6 mg Tablets- **CTD8995**
Cortimax 12 mg Tablets- **CTD8996**

9. Date of first authorization/renewal of the authorization
17/02/2023

10. Date of revision of the text
11/05/2025