SUMMARY OF PRODUCT CHARACTERISTICS

a) Proprietary name of a medicine

Predilone Tablets

b) Approved generic name(s)

Prednisolone BP

c) Qualitative and quantitative composition

Prednisolone 5 mg BP

d) Dosage form

Tablets

e) Clinical particulars

i. **Therapeutic indication(s)**

Prednisolone is a glucocorticoid given in the treatment of various disorders in which corticosteroids are indicated, except adrenal deficiency. It is indicated for states like bronchial asthma, severe hyper-sensitivity reactions, anaphylaxis, rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease, polyarteritis nodosa, inflammatory skin disorders, nephrotic syndrome, acute interstitial nephritis, ulcerative colitis, Crohn's disease, pulmonary sarcoid, rheumatic carditis, haemolytic anaemia, acute and lymphatic leukaemia, malignant lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura, immuno-suppression in transplantation.

ii. **Route of administration**

For oral use

Predilone tablets can be swallowed whole without difficulty or can be taken by dissolving in water. Dose: 5 to 60 mg i.e. 1 tablet to 12 tablets daily in divided doses, as a single daily dose after breakfast, or as a double dose on alternate days.

iii. **Contra-indications**

Patients with a history of hypersensitivity to prednisolone should not take predilone tablets.

Prednisolone is contra-indicated in the presence of acute infections uncontrolled by appropriate antimicrobial chemotherapy.

i. **Special warnings and precautions for use**

Prednisolone should be used with caution in the presence of congestive heart failure, recent myocardial infarction, or hypertension, in patients with diabetes mellitus, epilepsy, glaucoma, hypothyroidism, liver failure, osteoporosis, peptic ulceration, psychoses or severe affective disorders, and renal impairment. Children may be at increased risk of some adverse effects: in addition, corticosteroids may cause growth retardation, and prolonged administration is rarely justified. The elderly too may be at greater risk from adverse effects. Patients with active or doubtfully quiescent tuberculosis should not be given prednisolone except, very rarely, as

adjuncts to treatment with antitubercular drugs. Patients with quiescent tuberculosis should be observed closely and should receive chemoprophylaxis if prednisolone therapy is prolonged. The risks of chickenpox and probably of severe herpes zoster are increased in non-immune patients receiving therapeutic doses of systemic corticosteroids, and patients should avoid close personal contact with either infection. Passive immunization is recommended for non-immune patients who do come into contact with chickenpox. Similar precautions apply to measles. Live vaccines should not be given to patients receiving high-dose systemic corticosteroid therapy nor for at least 3 months afterwards: killed vaccines or toxoids may be given although the response may be attenuated. During prolonged courses of prednisolone therapy, patients should be examined regularly. Sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of the fluid intake and output, and daily weight records may give early warning of fluid retention. Back pain may signify osteoporosis. Children are at special risk from raised intracranial pressure.

When the treatment is to be discontinued, the dose should be reduced gradually over a period of several weeks or months depending on the dosage and duration of the therapy.

ii. **Interactions**

Antacids can reduce the absorption of prednisolone if given in high doses. Indigestion remedies should not be taken at the same time of day as Prednisolone.

- Rifampicin, rifabutin, carbamazepine, phenobarbital, phenytoin, primidone, carbimazole and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced. Therefore it may be necessary to adjust the dose of prednisolone accordingly.
- The desired effects of hypoglycemic agents (including insulin), antihypertensives and diuretics are antagonised by corticosteroids.
- The hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, beta-2-agonists, theophylline 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.
- Ciclosporin increases the plasma concentration of prednisolone.
- The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.
- NSAIDs such as indometacin may increase the risk of GI ulceration. The possibility of GI ulceration should be considered with concomitant use with any other NSAIDs.
- Antifungals: Increased risk of hypokalemia with amphotericin. Avoid concomitant use. Ketoconazole reduces the metabolic and renal clearances of methylprednisolone, this

may also occur with prednisolone.

- Mifepristone reduces the effect of corticosteroids for 3-4 days after administration.
- Methotrexate may have a steroid sparing effect. There is evidence that the toxicity of methotrexate is increased.
- Etoposide metabolism may be inhibited by corticosteroids in vitro. This may lead to an increase in both efficacy and toxicity of the etoposide. Monitoring would be prudent.
- Corticosteroids should not be used concurrently with retinoid and tetracyclines due to increased intracranial pressure.

- Estrogens and progestogens increase plasma concentrations of corticosteroids.

i. **Pregnancy and lactation**

The ability of corticosteroids to cross the placenta varies between individual drugs; however, 88% of prednisolone is inactivated as it crosses the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of fetal 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 and immunosuppression may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. Cataracts have also been rarely reported.

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. Patients with pre-eclampsia or fluid retention require close monitoring.

Corticosteroids are excreted in small amounts in breast milk. However doses of up to 40mg daily of prednisolone 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. Monitoring of the infant for adrenal suppression is advised.

ii. **Effects on the ability to drive and operate machinery**

If insufficient sleep occurs, the likelihood of impaired alertness may be increased; patients should make sure they are not affected before driving or operating machinery.

f) Pharmacological properties

i. Pharmacodynamic properties

ATC code H02AB06

Prednisolone is a glucocorticoid, which acts by controlling the rate of synthesis of proteins. It reacts with receptor proteins in the cytoplasm of sensitive cells in many tissues to form a steroid receptor complex. The complex undergoes a modification, as noted by an increase in the sedimentation constant, and then moves into the nucleus, where it binds to chromatin and regulates transcription of specific genes. Binding of it, by their receptor results in dissociation of a phosphorylated protein of approximately 90000 Dalton size from the receptor complex in the cytosol. The release of this intriguing protein plays a major part in the transformation of the receptor, enabling the hormone-receptor complex to proceed to its nuclear destination or to interact fruitfully with DNA

ii. Pharmacokinetic properties –

Prednisolone is readily absorbed from the gastro-intestinal tract. Peak plasma concentrations of prednisolone are obtained 1 or 2 hours after administration by mouth, and it has a usual plasma half-life of 2 to 4 hours. Its initial absorption, but not its overall bioavailability, is affected by food. Prednisolone is extensively bound to plasma proteins. The volume of distribution, and also the clearance are reported to increase with an increase from low to moderate doses: at very high doses, clearance appears to become saturated.

Prednisolone is excreted in the urine as free and conjugated metabolites, together with an appreciable proportion of unchanged prednisolone. Prednisolone crosses the placenta and small amounts are excreted in breast milk.

iii. Preclinical safety data – Not applicable.

g) Pharmaceutical particulars

i. List of excipients

Prednisolone

Starch

Lactose

Starch

Sodium Benzoate

Potassium Sorbate

Purified water

Magnesium stearate

ii. **Incompatibilities** - None known.

iii. **Shelf-life** -

- **In the original unopened container**; 48 months
- **After reconstitution (where appropriate)** NA
- **Shelf-life after first opening:** Not applicable

iv. **Special precautions for storage:** Store below 25°C in a dry place. Protect from light.

- **Nature and composition of containers** Blister pack in unit carton
- HDPE containers

v. **Instruction for use/handling** – Not applicable

vi. **Restriction on sale / distribution:** POM

h) Administrative data

i. **Name and address of holder of a registration.**

Regal Pharmaceuticals Limited

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Plot No.: 7879/18, Off Baba Dogo Road, Ruaraka,

P.O. Box 44421-00100, Nairobi, Kenya

ii. **Registration number**. H93/034

iii. **Date of first registration**- 03/11/1993

iv. **renewal of a registration certificate.**- 20/06/2007

DECLARATION BY AN APPLICANT

I, the undersigned certify that all the information in this form and accompanying documentation is correct, complete and true to the best of my knowledge.

I further confirm that the information referred to in my application dossier is available for verification during GMP inspection.

I also agree that I shall carry out pharmacovigilance to monitor the safety of the product in the market and provide safety update reports to the National Medicines Regulatory Authority of the EAC Partners States.

I further agree that I am obliged to follow the requirements of the Partner States Legislations and Regulations, which are applicable to medicinal products.

I also consent to the processing of information provided by the EAC Partner States.

It is hereby confirmed that fees will be paid/have been paid according to the National/Community rules*

Name: DR. MANDERE JAMES ATEBE
Position in the company: COMPANY PHARMACIST

Signature: .....

Date: 10th June 2019.

Official stamp:.....

* Note: If fees have been paid, attach proof of payment