Professional Information for Medicines for Human Use

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

BE-TABS PREDNISONE 5 mg (TABLETS)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg Prednisone.

Contains sugar (lactose monohydrate): 106 mg per tablet

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

White tablet 6,4 mm in diameter, biconvex with a score mark on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Suppressive and palliative therapy in **rheumatoid arthritis** which is progressive despite intensive conventional treatment.

The **nephrotic syndrome** attributable to systemic lupus erythematosus or to primary renal disease, except renal amyloidosis, may be benefited by corticosteroid therapy.

Collagen diseases. Manifestations of most of these diseases, except scleroderma are controlled. Morbidity is decreased and the survival times of patients with polyarteritis nodosa and Wegener's granulomatosis is prolonged.

Fulminating systemic lupus erythematosus is a life-threatening condition the manifestations of which should be promptly suppressed with large doses.

Manifestations of **allergic conditions** which do not react to anti-histaminic treatment may be suppressed by adequate doses or as a supplement to primary therapy. However, severe reactions such as anaphylaxis require immediate adrenalin subcutaneously.

Bronchial asthma. Acute, or severe chronic asthma, uncontrolled by other measures.

Acute skin diseases and exacerbations of chronic skin diseases. Severely ill patients with **chronic ulcerative colitis.**

Thrombocytopenia: To decrease the bleeding tendency.

Organ transplantations.

4.2 Posology and method of administration

1. The dose must be determined individually by the seriousness of the disease and the reaction of the patient.
2. Administration of large doses for short courses cause less side effects than long-term therapy with small doses. Long courses of therapy at high dosage should be reserved for life-threatening diseases.
3. In long-term therapy the dose must be the smallest one to achieve a desired effect. Complete relief is not sought.

Rheumatoid arthritis:

The initial dose should be small, usually about 10 mg and increase slowly until the desired degree

of control is attained.

Nephrotic syndrome:

60 mg Daily in divided doses (2 mg/kg oedema-free body mass in children) for 3 to 4 weeks. If a remission with a diuresis and decreased proteinuria occurs during this period, maintenance treatment is continued for as long as a year. For this the daily dose of prednisone is given only for the first 3 days of each week.

Collagen disease:

1 mg/kg daily until remission is induced. The dose is then reduced to the minimal effective level.

Fulminating systemic lupus erythematosus:

1 mg/kg daily which may be increased in 20 mg increment daily until a favourable response occurs. After control has been obtained, dosage should be reduced by small steps of 5 mg prednisone per week until further reductions elucidate symptoms.

Bronchial asthma:

In status asthmaticus the attack is brought under control by intravenous cortisol whereafter 10 mg prednisone is given for 4 to 5 days. The dose is then reduced in steps to be withdrawn 10 days after initiation of prednisone therapy.

Severe chronic bronchial asthma:

To reduce severity without eliminating the manifestations of the disease, 5 to 10 mg daily in divided doses in combination with the usual medication.

Skin diseases:

40 mg per day. Up to 120 mg per day may be life-saving in pemphigus.

Chronic ulcerative colitis:

60 to 120 mg per day.

Thrombocytopenia:

0,5 mg/kg.

Organ transplantation:

50 to 100 mg at the time of surgery. Maintenance doses of 10 to 20 mg per day are continued indefinitely and the dosage increased if rejection is threatened.

The dosage should be reduced and therapy discontinued gradually if therapy is continued for more then a few days. Abrupt cessation of prolonged, high dosage therapy may produce adrenal insufficiency or sufficient severity to be threatening to life.

4.3 Contraindications

- Known hypersensitivity to prednisone or to any of the excipients of **BE-TABS PREDNISONE 5 mg** (see section 6.1)
- Liver disease
- Peptic ulcer
- Osteoporosis
- Phychosis or severe phychoneurosis

- Because of interference with antibody formation, systemic administration is usually contra-indicated in the presence of acute bacterial and viral infections.

4.4 Special warnings and precautions for use

Corticosteroids should be used only with great caution in the presence of congestive heart failure, in patients with diabetes mellitus, infectious diseases, chronic renal failure, and uraemia, and in elderly persons. Patients with active or doubtfully quiescent tuberculosis should not be given these hormones except as adjuncts to treatment with tuberculostatic drugs. Patients with quiescent tuberculosis should be observed closely and should receive chemoprophylaxis if corticosteroid therapy is
prolonged.

Acute adrenal insufficiency may occur during prolonged treatment or on cessation of treatment and may be precipitated by an infection or stressful situation such as anaesthesia, surgery or trauma.

Patients under stress should therefore receive supplementary corticosteroids if they were given corticosteroids in the previous 3 months or high prolonged doses in the previous year. Infections may be masked. A reduction in the number of circulating lymphocytes may occur. Immunisation procedures should not be undertaken in patients receiving corticosteroids. Caution must be observed in ulcerative colitis if a possibility exists of intestinal perforation and peritonitis.

Bradycardia has been reported following high doses.

Pheochromocytoma-related crisis, which may be fatal, has been reported following systemic corticosteroid administration. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma following consideration of individual risk / benefit.

BE-TABS PREDNISONE 5 mg contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

BE-TABS PREDNISONE 5 mg contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction

Concurrent administration of barbiturates, phenylbutazone, phenytoin, or rifampicin may enhance the metabolism and reduce the effects of corticosteroids. Response to anticoagulants may also be reduced by corticosteroids.

4.6 Fertility, pregnancy and lactation

Babies born of mothers who received large doses corticosteroids during pregnancy should be watched carefully for signs of hypoadrenalism. Corticosteroids appear in breast milk and mothers receiving corticosteroids should be advised not to breast feed.

4.7 Effects on ability to drive and use machines

The effect of prednisolone on the ability to drive or use machinery has not been evaluated. There is no evidence to suggest that prednisolone may affect these abilities.

4.8 Undesirable effects

System Organ Class	Frequency	Adverse Reaction

Blood and lymphatic system disorders	Not known	An increase in the coagulability of the blood may lead to thrombo-embolic complications.
Metabolism and nutrition disorders	Not known	Retention of sodium and water, with oedema and hypertension; increased excretion of potassium with the possibility of hyperkalaemic alkalosis, and in extreme cases cardiac failure may be induced. Patients receiving diuretics which cause potassium depletion should be watched carefully for signs of hypokalaemia. Excessive metabolic effects which lead to mobilisation of Calcium and phosphorous, with osteoporosis and spontaneous fractures, nitrogen depletion, and hyperglycaemia with accentuation or precipitation of the diabetic state. Insulin requirements of diabetic patients are increased. Increased appetite.
Nervous system disorders	Not known	Mental and neurological disturbances, Intracranial hypertension
Cardiac disorders	Not known	Bradycardia.[1]
Gastrointestinal disorders	Not known	There may be peptic ulceration with haemorrhage and perforation.
Reproductive system and breast disorders	Not known	Amenorrhoea

General disorders and administration site conditions	Not known	An effect on tissue repair which is manifest in delayed wound healing and increased liability to infection.
Endocrine disorders	Not known	Pheochromocytoma-related crisis (see section 4.4)

[1].Following high doses.

On sudden reduction of dosage during the treatment of rheumatoid arthritis, fatalities have been attributed to lesions of small arterioles similar to polyarteritis.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting form",** found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/index/8

4.9 Overdose

Reports of acute toxicity and/or death following overdosage of glucocorticoids are rare. No specific antidote is available; treatment is supportive and symptomatic. Serum electrolytes should be monitored.

High systemic doses of corticosteroids caused by chronic use have been associated with adverse effects such as neuropsychiatric disorders (psychosis, depression, and hallucinations), cardiac dysrhythmias and Cushing's syndrome.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use. ATC code: H02AB06

Category and class: A 21.5.1 Corticosteroids and Analogues.

Prednisone is a synthetic glucocorticoid which produces various metabolic effects and in addition modifies the immune reaction of the body to diverse stimuli. It has properties qualitatively similar to those of cortisone acetate but causes less sodium and fluid retention and is therefore preferred in the treatment of such conditions as asthma, psoriasis, rheumatoid arthritis, thrombocytopenia and ulcerative colitis. Prednisone is not used for adrenal-deficiency states. It is useful in the treatment of the nephrotic syndrome. Prednisone is inactive until converted to prednisolone in the liver.

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt – retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Glucocorticoid cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

5.2 Pharmacokinetic properties

Prednisolone is rapidly and apparently almost completely absorbed after oral administration; it reaches peak plasma concentrations after 1-3 hours. There is however wide inter-subject variation suggesting impaired absorption in some individuals. Plasma half – life is about 3 hours in adults

and somewhat less in children, Its initial absorption, but not its overall bioavailability, is affected by food. Prednisolone has a biological half-life lasting several hours, making it suitable for alternate-day administration regimens.

Although peak plasma prednisolone levels are somewhat lower after administration of prednisolone tablets and absorption is delayed, total absorption and bioavailability is delayed, total absorption and bioavailability are the same as after plain prednisolone. Prednisolone shows dose dependent pharmacokinetics, with an increase in dose leading to an increase in volume of free, pharmacologically active drug. Reduced doses are necessary in patients with hypoalbuminaemia.

Prednisolone is metabolised primarily in the liver to a biologically inactive compound. Liver disease prolongs the half-lifeof prednisolone and, if the patient has hypoalbuminaemia, also increases the proportion of unbound drug and may thereby increase adverse effects.

Prednisolone is excreted in the urine as free and conjugated metabolites, together with small amounts of unchanged prednisolone.

Significant differences in the pharmacokinetics of prednisolone amongst menopausal women have been described. The postmenopausal women had reduced unbound clearance (30 %), reduced total clearance and increased half-life of prednisolone.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Lactose monohydrate
- Magnesium Stearate
- Microcrystalline Cellulose
- Pregelatinised Starch
- Sodium Starch Glycolate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months – 100, 500 and 1000 in a securitainer, 500's and 1000's in a white HDPE bottle and 5000 tablets in a white HDPE jar.

15 Months – Patient ready packs of different pack sizes.

6.4 Special precautions for storage

Store in a cool dry place, at or below 25 °C, protect from light.

6.5 Nature and contents of container

100, 500 and 1000 in a securitainer, 500's and 1000's in a white HDPE bottle and 5000 tablets in a white HDPE jar. Patient ready packs of different pack sizes.

6.6 Special precautions for disposal

No special requirements for disposal.

7. HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 Lautre Road,

Stormill, Ext.1,

Roodepoort, 1724

South Africa

8. REGISTRATION NUMBER(S)

G 3004 (Act 101 of 1965)

NS2	021001382 (Namibia)
Botswana List No.: B9315040	

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

September 1985

10. DATE OF REVISON OF THE TEXT

23 December 2022