

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCTS

PREDNIFIL (Prednisolone Tablets BP 5 mg)

2. QUALITY AND QUANTITATIVE COMPOSITION

Each tablet contains 5mg of Prednisolone

Excipients with known effect

Each tablet contains 53.88 mg of lactose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White, flat, circular, uncoated tablets with a break line on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Allergy and anaphylaxis: bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema, anaphylaxis.

Arteritis/collagenosis: giant cell arteritis/polymyalgia rheumatica, mixed connective tissue disease, polyarteritis nodosa, polymyositis.

Blood disorders: haemolytic anaemia (auto-immune), leukaemia (acute and chronic lymphocytic), lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura.

Cardiovascular disorders: post-myocardial infarction syndrome, rheumatic fever with severe carditis.

Endocrine disorders: primary and secondary adrenal insufficiency, congenital adrenal hyperplasia.

Gastro-intestinal disorders: Crohn's disease, ulcerative colitis, persistent coeliac syndrome (coeliac disease unresponsive to gluten withdrawal), auto-immune chronic active hepatitis, multisystem disease affecting liver, biliary peritonitis.

Hypercalcaemia: sarcoidosis, vitamin D excess.

Infections (with appropriate chemotherapy): helminthic infestations, Herxheimer reaction, infectious mononucleosis, miliary tuberculosis, mumps orchitis (adult), tuberculous meningitis, rickettsial disease.

Muscular disorders: polymyositis, dermatomyositis.

Neurological disorders: infantile spasms, Shy-Drager syndrome, sub-acute demyelinating polyneuropathy.

Ocular disease: scleritis, posterior uveitis, retinal vasculitis, pseudo-tumours of the orbit, giant cell arteritis, malignant ophthalmic Grave's disease.

Renal disorders: lupus nephritis, acute interstitial nephritis, minimal change glomerulonephritis.

Respiratory disease: allergic pneumonitis, asthma, occupational asthma, pulmonary aspergillosis, pulmonary fibrosis, pulmonary alveolitis, aspiration of foreign body, aspiration of stomach contents, pulmonary sarcoid, drug induced lung disease, adult respiratory distress syndrome, spasmodic croup.

Rheumatic disorders: rheumatoid arthritis, polymyalgia rheumatica, juvenile chronic arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease.

Skin disorders: pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, pyoderma gangrenosum.

Miscellaneous: sarcoidosis, hyperpyrexia, Behçets disease, immunosuppression in organ transplantation.

4.2 Posology and method of administration

General

The following therapeutic guidelines should be kept in mind for all therapy with corticosteroids:

Corticosteroids are palliative symptomatic treatment by virtue of their anti-inflammatory effects; they are never curative.

The appropriate individual dose must be determined by trial and error and must be re-evaluated regularly according to activity of the disease.

As corticosteroid therapy becomes prolonged and as the dose is increased, the incidence of disabling side-effects increases.

In general, initial dosage shall be maintained or adjusted until the anticipated response is observed. The dose should be gradually reduced until the lowest dose which will maintain an adequate clinical response is reached. Use of the lowest effective dose may also minimise side-effects (see section 4.4).

In patients who have received more than physiological dose for systemic corticosteroids (approximately 7.5mg prednisolone 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 hypothalamic-pituitary-adrenal (HPA) suppression, the dose of corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 7.5mg of prednisolone 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 40mg daily of prednisolone, 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 40mg daily of prednisolone (or equivalent).
- Patients repeatedly taking doses in the evening.

See also sections 4.4 and section 4.8.

During prolonged therapy, dosage may need to be temporarily increased during periods of stress or during exacerbations of the disease (see section 4.4)

If there is lack of a satisfactory clinical response to prednisolone, the drug should be gradually discontinued and the patient transferred to alternative therapy.

Posology

Adults including the elderly

The lowest effective dose should be used for the minimum period in order to minimise side effects (see section 4.4)

Initially:

The initial dosage may vary from 5mg to 60mg daily in divided doses, as a single dose in the morning after breakfast, or as a double dose on alternate days. Dosage depends on the disorder being treated. The dose can often be reduced within a few days but may need to be continued for several weeks or months.

Maintenance:

2.5 to 15mg daily, but higher doses may be needed. Cushingoid side-effects more likely above 7.5mg daily.

Posology for specific indications

Intermittent dosage regimen: A single dose of prednisolone in the morning on alternate days or at longer intervals is acceptable therapy for some patients. When this regimen is practical, the degree of pituitary-adrenal suppression can be minimised.

Specific dosage guidelines: The following recommendations for some corticosteroid-responsive disorders are for guidance only. Acute or severe disease may require initial high dose therapy with reduction to the lowest effective maintenance dose as soon as possible. Dosage reductions should not exceed 5-7.5mg daily during chronic treatment.

Allergic and skin disorders: Initial doses of 5-15mg daily are commonly adequate.

Collagenosis: Initial doses of 20-30mg daily are frequently effective. Those with more severe symptoms may require higher doses.

Rheumatoid arthritis: The usual initial dose is 10-15mg daily. The lowest daily maintenance dose compatible with tolerable symptomatic relief is recommended.

Blood disorders and lymphoma: An initial daily dose of 15-60mg is often necessary with reduction after an adequate clinical or haematological response. Higher doses may be necessary to induce remission in acute leukaemia.

Special populations

Elderly

Treatment of elderly patients, particularly if long-term, should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age (see section 4.4).

Children

Although appropriate fractions of the actual dose may be used, dosage will usually be determined by clinical response as in adults. Prednisolone should be used only when specifically indicated, in a minimal dosage and for the shortest possible time (see sections 4.4 and 4.8)

Method of administration

Tablets for oral administration. The tablets should be taken with or after food.

4.3 Contraindications

Except where its use may be life-saving, prednisolone must be used with great caution in patients with the following conditions – peptic ulcer, Osteoporosis, infections, diabetes mellitus and psychological disorders.

4.4 Special warnings and precautions for use

Sudden withdrawal or reduction in dosage, or an increase in corticosteroid requirements associated with the stress of infection, or accidental or surgical trauma may cause acute adrenal insufficiency. Symptoms of adrenal insufficiency include malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration.

In patients on glucocorticoid therapy subjected to unusual stress, increased dosage of rapidly acting steroids before, during, and after the stressful situation is indicated.

Glucocorticoids may mask some signs of infection and new infections may appear during their use.

There may be decreased resistance and inability to localize infection when glucocorticoids are used.

The use of Prednisolone tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the glucocorticoid is used for the management of the disease in conjunction with an appropriate antituberculous 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.

Immunization procedures should not be undertaken in patients who are on glucocorticoids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

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.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives such as Prednisolone except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All glucocorticoids increase calcium excretion.

4.5 Interaction with other medicinal products and other forms of interaction

Antacids	The absorption of prednisolone may be reduced by large doses of some antacids such as magnesium trisilicate or aluminium hydroxide.
Antibacterials	Rifamycins accelerate metabolism of corticosteroids and thus may reduce their effect. Erythromycin inhibits metabolism of methylprednisolone and possibly other corticosteroids. Prednisolone can lower plasma levels of isoniazid. Where a reduced response during concurrent use is noted, dosage adjustment of isoniazid may be necessary.
Anticoagulants	Response to anticoagulants may be reduced or, less often,

	enhanced by corticosteroids. Close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.
Antidiabetic agents	Glucocorticoids may increase blood glucose levels. Patients with diabetes mellitus receiving concurrent insulin and/or oral hypoglycemic agents may require dosage adjustments of such therapy.
Antiepileptics	Carbamazepine, phenobarbital, phenytoin, and primidone accelerate metabolism of corticosteroids and may reduce their effect.
Antifungals	Risk of hypokalaemia may be increased with amphotericin, therefore concomitant use with corticosteroids should be avoided unless corticosteroids are required to control reactions; ketoconazole inhibits metabolism of methylprednisolone and possibly other corticosteroids.
Antimuscarinics (Anticholinergics)	Prednisolone has been shown to have antimuscarinic activity. If used in combination with another antimuscarinic drug could cause impairment to memory and attention in the elderly.
Antithyroids	Prednisolone clearance increased by the use of carbimazole and thiamazole.
Antiviral	Plasma concentrations of prednisolone may be increased with antiviral drugs such as ritonavir and indinavir.
Cardiac Glycosides	Increased toxicity if hypokalaemia occurs with corticosteroids.
Ciclosporin	Concomitant administration of prednisolone and ciclosporin may result in decreased plasma clearance of prednisolone (i.e. increased plasma concentration of prednisolone). The need for appropriate dosage adjustment should be considered when these drugs are administered concomitantly.
Cytotoxics	Increased risk of haematological toxicity with methotrexate.
Hepatic microsomal enzyme inducers	Drugs that induce hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4 such as phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminoglutethimide may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism. Lack of expected response may be observed and dosage of Deltacortril Gastro-resistant Tablets may need to be increased.
Hepatic microsomal enzyme inhibitors	Drugs that inhibit hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4 (e.g. ketoconazole, troleandomycin) may decrease glucocorticoid clearance. Dosages of glucocorticoids given in combination with such drugs may need to be decreased to avoid potential adverse effects.
Hormonal contraceptives	Oral contraceptives increased prednisolone concentrations by 131%. May increase AUC and reduce clearance in oral contraceptives containing ethinylestradiol, mestranol, desogestrel, levonorgestrel, norgestrel or norethisterone.
Immunosuppressants	Tumorigenicity: direct tumour-inducing effects of the glucocorticoids are not known, but the particular risk that malignancies in patients undergoing immunosuppression with these or other drugs will spread more rapidly is a well-recognised problem. Mutual inhibition of metabolism may occur between ciclosporin and prednisolone, and may increase the plasma concentration of either drug.

Liquorice	Glycyrrhizin can delay the clearance of prednisolone
Mifepristone	Effect of corticosteroids may be reduced for 3-4 days after mifepristone
Non-steroidal anti-inflammatory drugs	Concomitant administration of ulcerogenic drugs such as indomethacin during corticosteroid therapy may increase the risk of GI ulceration. Aspirin should be used cautiously in conjunction with glucocorticoids in patients with hypoprothrombinaemia. Although concomitant therapy with salicylate and corticosteroids does not appear to increase the incidence or severity of GI ulceration, the possibility of this effect should be considered. Serum salicylate concentrations may decrease when corticosteroids are administered concomitantly. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Salicylates and corticosteroids should be used concurrently with caution. Patients receiving both drugs should be observed closely for adverse effects of either drug.
Oestrogens	Oestrogens may potentiate the effects of glucocorticoids and dosage adjustments may be required if oestrogens are added to or withdrawn from a stable dosage regimen.
Protease inhibitors	Ritonavir possibly increases plasma concentrations of prednisolone and other corticosteroids by reduction in clearance of prednisolone through the inhibition of P450 isoenzyme CYP3A4.
Other	The desired effects of hypoglycaemic agents (including insulin), antihypertensives and diuretics are antagonised by corticosteroids; and the hypokalaemic effect of acetazolamide, loop diuretics, thiazide diuretics, carbenoxolone and theophylline are enhanced.
Somatropin	Growth promoting effect may be inhibited.
Sympathomimetics	Increased risk of hypokalaemia if high doses of corticosteroids given with high doses of bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline.

4.6 Fertility, Pregnancy and lactation

Pregnancy

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 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. The use of corticosteroids, including prednisolone, during pregnancy may also result in stillbirth. Hypoadrenalism 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 been observed in infants born to mothers treated with long-term prednisolone during pregnancy. 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

Breast-feeding

Corticosteroids are excreted in small amounts in breast milk. Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants.

Since adequate reproductive studies have not been performed in humans with glucocorticoids, these drugs should be administered to nursing mothers only if the benefits of therapy are judged to outweigh the potential risks to the infant.

The concentration of the steroid in the milk can be between 5 and 25% of those in the serum and the two roughly parallel one another after an oral dose.

There are no reports found regarding neonatal toxicity following exposure to corticosteroids during lactation, however if maternal doses >40mg/day of prednisolone is prescribed, the infant should be monitored for adrenal suppression.

4.7 Effects on ability to drive and use machines

The effect of Prednisolone Tablets 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

a) Summary of the safety profile

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.

b) Tabulated list of adverse reactions

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).

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

Very common: $\geq 1/10$

Common: $\geq 1/100$ to $< 1/10$

Uncommon: $\geq 1/1,000$ to $< 1/100$

Rare: $\geq 1/10,000$ to $< 1/1,000$

Very rare: $< 1/10,000$

Not known: cannot be estimated from the available data

System Organ Class	Frequency	Undesirable Effect
Infections and Infestations	Not known	Increases susceptibility to, and severity of infections ¹ , opportunistic infections, recurrence of dormant tuberculosis ² , oesophageal candidiasis.

Blood and lymphatic system disorders	Not known	Leucocytosis
Immune system disorders	Not known	Hypersensitivity including anaphylaxis.
Endocrine disorders	Not known	Suppression of the hypothalamo-pituitary adrenal axis ³ , cushingoid facies, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of latent diabetes mellitus.
Metabolism and nutrition disorders	Not known	Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen and calcium balance, glucose intolerance and protein catabolism. Increase both high and low density lipoprotein cholesterol concentration in the blood. Increased appetite ⁴ . Weight gain, obesity, hyperglycaemia, dyslipidaemia.
	Very rare	Calciophylaxis ⁵
Psychiatric disorders	Common	Irritability, depressed and labile mood, suicidal thoughts, psychotic reactions, mania, delusions, hallucinations, and aggravation of schizophrenia. behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion, restlessness, nervousness and amnesia.
	Not known	Euphoria, psychological dependence, depression.
Nervous system disorders	Not known	Depression, insomnia, dizziness, headache, vertigo. Raised intracranial pressure with papilloedema (pseudotumor cerebri) ⁶ . Aggravation of epilepsy, epidural lipomatosis. vertebrobasilar stroke ⁷
Eye disorders	Not known	Glaucoma, papilloedema, posterior subcapsular cataracts, nuclear cataracts (particularly in children), exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease. Severe exacerbation of bullous exudative retinal detachment; lasting visual loss in some patients with idiopathic central serous chorioretinopathy. ⁸
Ear and labyrinth disorders	Not known	Vertigo.
Cardiac disorders	Not known	Congestive heart failure in susceptible patients, hypertension, increased risk of heart failure. Increased risk of cardiovascular disease, including myocardial infarction. ⁹ Bradycardia. ¹⁰
Vascular disorders	Not known	Thromboembolism
Gastrointestinal disorders	Not known	Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, diarrhoea, oesophageal ulceration, acute pancreatitis.
Skin and subcutaneous tissue disorders	Not known	Hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, pruritus, rash, urticaria
Musculoskeletal and connective tissue disorders	Not known	Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, tendinopathies (particularly of the Achilles and patellar tendons), myalgia, growth suppression in infancy, childhood and adolescence.
Renal and urinary	Not known	Scleroderma renal crisis*

disorders		
Reproductive system and breast disorders	Not known	Menstrual irregularity, amenorrhoea.
General disorders and administration site conditions	Not known	Fatigue, malaise, impaired healing
Investigations	Not known	Increased intra-ocular pressure, may suppress reactions to skin tests.

* see section c)

1. with suppression of clinical symptoms and signs.
2. see section 4.4.
3. particularly in times of stress, as in trauma, surgery or illness.
4. which may result in weight gain.
5. see section 4.4.
6. usually after treatment withdrawal.
7. exacerbation of giant cell arteritis, with clinical signs of evolving stroke has been attributed to prednisolone.
8. see section 4.4.
9. with high dose therapy.
10. Following high doses.

c) Description of selected adverse events

Withdrawal symptoms

Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4). A steroid 'withdrawal syndrome' seemingly unrelated to adrenocortical insufficiency may also occur following abrupt discontinuance of glucocorticoids. This syndrome includes symptoms such as: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, weight loss, and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels. Psychological effects have been reported on withdrawal of corticosteroids.

Scleroderma renal crisis

Amongst the different subpopulations the occurrence of scleroderma renal crisis varies. The highest risk has been reported in patients with diffuse systemic sclerosis. The lowest risk has been reported in patients with limited systemic sclerosis (2%) and juvenile onset systemic sclerosis (1%).

Reporting of suspected adverse reactions

Assess and comment on therapeutic indications posology and method of administration, contraindications, special warnings and precautions for use, interactions, pregnancy and lactation, effects on ability to drive and use machines, undesirable effects and overdose. If the applicant is proposing different clinical particulars from the comparator, request for justification and clinical data to support their claims.

Standard low-dose therapy with prednisolone is generally free from untoward symptoms. On a long-term basis, however, minor gastrointestinal disturbances, such as nausea and vomiting may occur. Nocturia is fairly common during corticosteroid

treatment. Increased appetite, obesity, facial rounding and fragility of skin are some of the prime indicators of glucocorticoid over - activity.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. 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

Brief Clinical description of symptoms

A single large dose of prednisolone is not expected to produce life-threatening symptoms. However, long-term use of high steroid doses can lead to symptoms such as thinning skin, easy bruising, changes in the shape or location of body fat (especially in your face, neck, back, and waist), increased acne or facial hair, menstrual problems, impotence, or loss of interest in sex.

Treatment of Overdosage:

Seek emergency medical attention if you think you have received too much of this medicine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use.

ATC code: H02AB06

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.

Glucocorticoids 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-life of 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.

5.3 Preclinical safety data

Teratogenic effects of glucocorticoids have not been demonstrated in the human. Although malignancies are known to arise in patients undergoing immunosuppression with corticosteroids, any role of these compounds in the induction of tumours remain uncertain. The classic toxic effects of prednisolone like drugs are given under adverse reactions.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

S.No	Ingredients	Reference
1	Lactose monohydrate	BP
2	Starch (mixing)	BP
3	Colloidal Anhydrous Silica (mixing)	BP
4	Starch (paste)	BP
5	Methyl Hydroxybenzoate	BP
6	Propyl Hydroxybenzoate	BP
7	Sodium Lauryl Sulphate	BP
8	Sodium Starch Glycolate	BP
9	Starch (lubrication)	BP
10	Colloidal Anhydrous Silica (lubrication)	BP
11	Purified Talc	BP
12	Magnesium Stearate	BP
13	Adipic Acid	BP
14	Purified Water	BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 months

6.4 Special Precautions for storage

Store below 30°C, in a dry place. Protect from light.

6.5 Nature and contents of container

Nature: 10 Blister strip of 10 tablets packed in a carton along with product literature.

Contents of container: 10x10's.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE

ADDRESSES:

M/S. Fourrts (India) Laboratories Pvt. Limited,

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8. MARKETING AUTHORIZATION NUMBER

H2004/8788/R1

9. DATE OF FIRST REGISTRATION / RENEWAL OF THE REGISTRATION

14.07.2009

10. DATE OF REVISION OF THE TEXT

11.08.2025