



National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. NAME OF THE MEDICINAL PRODUCT

Product Name : JPSONE

Generic Name : Prednisolone Tablet BP 5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains :

Prednisolone BP.....5 mg

Excipients.....q.s.

List of excipients :

Lactose

Maize Starch

Microcrystalline Cellulose

Purified Talc

Maize Starch

PVPK-30

Magnesium Stearate

Sodium Starch Glycolate

3. PHARMACEUTICAL FORM

Tablet

White, Circular, Flat, Bevelled, Uncoated Tablet Having A Breakline On One Side & Plain On Other Side.

4. Clinical particulars

4.1 Therapeutic indications

JPSONE (PREDNISOLONE TABLET BP 5 MG) is indicated

Allergy and anaphylaxis: bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema, anaphylaxis, incapacitating allergies unresponsive to conventional treatment.

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: regional ileitis (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 Graves disease.

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

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, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculosis chemotherapy.

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

Skin disorders: pemphigus vulgaris, exfoliative dermatitis, 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.

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.

During prolonged therapy, dosage may need to be temporarily increased during periods of stress or during exacerbations of the disease.

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

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.

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.

Method of administration

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

Adults, the elderly, and children and adolescents over 12 years of age:

If in children and adolescents, between the age of 12 and 18 years, this medicinal product is required for more than 3 days, or if symptoms worsen, a doctor should be consulted.

For adults aged 18 years or older the minimum effective dose should be used for the shortest time necessary to relieve symptoms. If the product is required for more than 10 days or if the symptoms worsen, or persist, the patient should consult a pharmacist or a doctor.

1 or 2 tablets to be taken up to three times a day, as required. The tablets should be taken with water. Leave at least 4 hours between doses and do not take more than 1200mg (6 tablets) in any 24 hour period. Not to be given to children under 12 years of age.

4.3 Contraindications

Hypersensitivity to prednisolone

JPSONE is contra-indicated in patients with systemic fungal infections unless considered

Life-saving. Systemic administration of corticosteroids is contra-indicated in patients with peptic

Ulcer. Osteoporosis. Psychoses and psychoneuroses, active or doubtfully quiescent

tuberculosis and acute infections.

Immunizations using live vaccines are contra-indicated in patients on corticosteroid therapy.

4.4 Special warnings and precautions for use

A patient information leaflet should be supplied with this product. Patients should carry "steroid treatment" cards which give clear guidance on the precautions to be taken to minimise risk and provide details of prescriber, drug, dosage and duration of treatment.

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 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.

Caution is necessary when corticosteroids, including prednisolone, are prescribed to patients with the following conditions and frequent patient monitoring is necessary:

- Diabetes mellitus or in those with a family history of diabetes.
- Glaucoma or in those with a family history of glaucoma.
- Hypertension or congestive heart failure.
- Liver failure.
- Epilepsy.
- Osteoporosis: This is of special importance in post-menopausal females who are at particular risk.
- Patients with a history of severe affective disorders and particularly those with a previous history of corticosteroid induced psychoses.
- Peptic ulceration.
- Previous steroid myopathy.
- Glucocorticoids should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy.
- Because cortisone has been reported rarely to increase blood coagulability and to precipitate intravascular thrombosis, thromboembolism, and thrombophlebitis, corticosteroids should be used with caution in patients with thromboembolic disorders.
- Renal insufficiency.
- Tuberculosis: Those with a history of, or X-ray changes characteristic of tuberculosis. The emergence of active tuberculosis can, however, be prevented by the prophylactic use of antituberculous therapy.
- Recent myocardial infarction (rupture).
- Chickenpox: 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 special care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.
- Measles: Patients are advised to avoid exposure to measles, medical advice should be sought if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.
- 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.
- The effect of corticosteroids may be enhanced in patients with hypothyroidism in those with chronic liver disease with impaired hepatic function.
- Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.
- Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment.

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.

Scleroderma renal crisis

Caution is required in patients with systemic sclerosis because of an increased incidence of (possibly fatal) scleroderma renal crisis with hypertension and decreased urinary output observed with a daily dose of 15 mg or more prednisolone. Blood pressure and renal function (s-creatinine) should therefore be routinely checked. When renal crisis is suspected, blood pressure should be carefully controlled.

Withdrawal

In patients who have received more than physiological doses of 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 HPA suppression, the dose of systemic 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,
- 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 reintroduced.

Use in children:

Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible and therefore long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, treatment should be limited to the minimum suppression of the hypothalamo-pituitary adrenal axis and growth retardation. The growth and development of infants and children should be closely monitored. Treatment should be administered where possible as a single dose on alternate days.

Use in the 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, especially osteoporosis, diabetes, hypertension, hypokalaemia, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life threatening reactions.

Excipients

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

4.5 Interaction with other medicinal products and other forms of interaction

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.

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 Prednisolone 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.

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.

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.

Antibacterials: Rifamycins accelerate metabolism of corticosteroids and thus may reduce their effect. Erythromycin inhibits metabolism of methylprednisolone and possibly other corticosteroids.

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.

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.

Antivirals: Ritonavir possibly increases plasma concentrations of prednisolone and other corticosteroids.

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.

Mifepristone: Effect of corticosteroids may be reduced for 3-4 days after mifepristone.

Vaccines: Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

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.

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.

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.

Corticosteroids should not be used concurrently with retinoids and tetracyclines due to increased intracranial pressure.

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.

4.6 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 affects 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 intrauterine growth retardation. Hypoadrenalism may 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 abnormal pregnancies may be treated as though they were in the non-gravid state.

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

Lactation

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.

4.7 Effects on ability to drive and use machines

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.

4.8 Undesirable effects

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 Not known.

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 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.

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, hypokalaemia 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
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
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.
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.
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 disorders	Not known	Scleroderma renal crisis*
Reproductive system and breast	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.

With suppression of clinical symptoms and signs
 Particularly in times of stress, as in trauma, surgery or illness.
 Which may result in weight gain.

Usually after treatment withdrawal.

Exacerbation of giant cell arteritis, with clinical signs of evolving stroke has been attributed to prednisolone with high dose therapy.) 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. 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

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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Glucocorticoid

ATC code: H02AB06

Synthetic glucocorticoid with anti-inflammatory, immunosuppressive and antiallergic action.

Prednisolone has, by weight, 4-5 times higher anti-inflammatory effect than cortisone, but affects electrolyte turnover to a lesser extent.

The mechanism of action is not yet fully understood.

5.2 Pharmacokinetic properties

Absorption

Prednisolone is rapidly absorbed into the gastrointestinal tract when given orally. Maximum plasma concentration is achieved after 1 to 2 hours after oral administration. The plasma half-life is normally 2 to 4 hours. Its initial absorption, but not total bioavailability, is affected by food.

Distribution

Prednisolone is highly bound to plasma proteins and has high affinity for the transcortin.

The volume of distribution and clearance are reported to increase with transition from low to medium doses.

Metabolism

Prednisolone is metabolised primarily in the liver to a biologically inactive compound.

Prednisolone can be reversibly converted to prednisone by 11 β -hydroxysteroid dehydrogenase.

The absolute bioavailability of prednisolone is on average 82% compared to intravenously administered prednisolone following a single 10 mg dose. At normal dosing, the effective duration is calculated to be 12-36 hours.

Elimination

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

More than 90% of the given amount is excreted in the urine. 7-15% is excreted in unchanged form.

5.3 Preclinical safety data

In animal experiments, corticosteroids have been shown to give rise to various types of malformations (palate gap, skeletal malformations). After long-term treatment, reduced placental and birth weight have been observed in animals.

Corticosteroids have been shown to reduce fertility when administered to the rat.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize Starch
Microcrystallin Cellulose
Purified Talc
Maize Starch
PVPK - 30
Magnesium Stearate
Sodium Starch Glycolalte

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Keep the blister packs in the outer carton in order to protect from light.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

10 tablets are packed in 1 blister strips, such a 10 blister strips are packed are in 1 mono carton.

6.6 Special precautions for disposal <and other handling>

Not available

7. <APPLICANT/MANUFACTURER>

MANUFACTURE NAME :

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