SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Prednisolone 1 mg Tablets BP.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1 mg Prednisolone.

Also contains lactose. For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Uncoated Tablets

White, circular, biconvex, tablets or white, circular, biconvex tablets embossed PV on one face and P over 1 on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prednisolone is indicated in the management of all condition that benefits from short or long term of glucocorticoid therapy. This includes:

Allergic states: Severe, incapacitating allergies unresponsive to conventional treatment; asthma including status asthmaticus, asthma serum sickness; drug hypersensitivity reactions.

Collagen disorders: Eg: systemic lupus erythematosus, polyarteritis nodosa, polymyositis, polymyalgia rheumatica and temporal (giant cell) arteritis, mixed connective tissue disease syndrome, acute rheumatic carditis.

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

Endocrine disorder: Primary and secondary adrenal insufficiency, congenital adrenal hyperplasia.

Rheumatic disorders: Usually given as an adjunctive therapy for short term administration during an acute episode or exacerbation of rheumatoid arthritis, psoriatic arthritis.

Hypercalcaemia: Sarcoidosis, vitamin D excess.

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

Muscular disorder: Polymyositis, dermatomyositis.

Neurological disorder: infantile spasm, 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's disease.

Renal disorder: Lupus nephritis, acute interstitial nephritis, minimal change nephritic syndrome.

Skin disorder: Life-threatening or incapacitating skin conditions such as pemphigus vulgaris, bullous pemphigoid, systematic lupus erythematosus, pyoderma gangrenosum and exfoliative dermatitis.

Neoplastic disease: Leukaemias and lymphomas in adults, acute leukaemia of childhood.

Gastro-Intestinal disease: During acute exacerbation in ulcerative colitis and regional ileitis (Crohn's Disease), persistent coeliac syndrome (coeliac disease unresponsive to gluten withdrawal), auto-immune chronic active hepatitis, multisystem disease affecting lever, biliary peritonitis.

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

Rheumatic Disorder: Rheumatoid arthritis disorder, polymyalgia, rheumatica, juvenile chronic arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease.

Blood disorders: Various blood dyscrasias eg: selected cases of haemolytic anaemia, thrombocytopenic purpura, leukaemia (acute and chronic lymphocytic) malignant lymphoma, multiple myeloma.

Miscellaneous: Sarcoidosis, hyperpyrexia, behcets disease immuno-supression in organ transplants.

4.2 Posology and method of administration

See section on special warnings and precautions for use.

Adult: Dosage may vary from 5mg to 60mg daily, initially, depending upon the disorder being treated, reducing gradually to maintenance level when symptoms have subsided. Maintenance dosage is usually 5-20mg daily reached in about two weeks by reduction of the daily dosage by 5mg or 2.5mg, two or three times a week.

Use of the lowest effective dose may also minimise side-effects (see Section 4.4).

When the drug is stopped it should be withdrawn gradually.

Intermittent dosage regimen: A single dose of prednisolone tablets in the morning on alternative 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 reduction should not exceed 5 – 7.5mg daily during chronic treatment.

Allergic and skin disorders: Initial dose of 5 – 15mg daily.

Collagenosis: Initial doses of 20 – 30mg daily. Those with more severe symptoms may require higher doses.

Rheumatoid arthritis: 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 of 15 – 60mg is often necessary with reduction after an adequate clinical or haematological response, higher dose may be necessary to induce remission in acute leukaemia.

Children:

Although appropriate fraction of the actual dose may be used, dosage will usually be determined by clinical response as in adults. Treatment should be limited to the minimum dosage for the shortest possible as a single dose on alternative days.

Children: Aged 1-6 years- One quarter the adult dose.

Aged 7-11 years- One half the adult dose.

Aged 12-17 years- Three quarters the adult dose.

Corticosteroids cause growth retardation in infancy, childhood and adolescence which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimise suppression of the hypothalamo-pituitary adrenal axis and growth retardation, treatment should be administered where possible as a single dose on alternate days.

Elderly: Treatment should be planned, especially in long-term administration, bearing in mind the more serious consequences of the common side effects of corticosteroids in old age (see also section 4.4), especially osteoporosis, diabetes, hypertension, hypokalaemia, osteoporosis, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

Administration: Oral; the tablets should be swallowed with a drink of water.

Withdrawal of the product

In patients who have received more than physiological doses of systemic corticosteroids (approximately 7.5 mg 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 uncertainly about HPA suppression, the dose of systemic

Corticosteroids but there are uncertainty about HPA suppression, the dose of systemic corticosteroids may be reduced rapidly to physiological doses. Once a daily dose equivalent to 7.5 mg 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 40 mg 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 patients 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 corticosteroids greater than 40 mg daily of prednisolone (or equivalent),
- 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 re-introduced.

4.3 Contraindications

Use in patients with peptic ulcer, active tuberculosis, acute psychosis or systemic infection unless specific anti-infective therapy is employed.

Use in patients hypersensitive to any ingredient.

Patients with ocular herpes simplex due to the possibility of perforation.

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

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 which provide details of prescriber, drug, dosage and the duration of treatment.

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 (see section 4.2)

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 them or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations (see Section 4.8).

Anti-Inflammatory/Immunosuppressive Effects

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 immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

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 take particular care avoid exposure to measles, immediate medical advice should be sought if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.

Tuberculosis: Caution is necessary and frequent monitoring required when prescribing corticosteroids for patients with a history of tuberculosis or X-ray changes characteristic of tuberculosis**.** The emergence of active tuberculosis can be prevented by the prophylactic use of anti-tuberculosis therapy.

Administration of Live Vaccines: Live vaccines should not be given to individuals on high doses of corticosteroids, due to impaired immune response. Live vaccines should be postponed until at least 3 months after stopping corticosteroid therapy. (See also Section 4.5). The antibody response to other vaccines may be diminished.

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 (see Section 4.5).

Adrenocortical Insufficiency

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration and duration of glucocorticoid therapy.

In addition, acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly. Drug induced secondary adrenocortical insufficiency may therefore be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently. During prolonged therapy an 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.

Special Precautions

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.

• Idiopathic central serious chorioretinopathy; glucocorticoid treatment can cause severe exacerbation of bullous exudative retinal detachment and lasting visual loss in some patients (see Section 4.8)

• Hypertension or congestive heart failure.

• Liver failure - Corticosteroid effects may be enhanced in those with chronic liver disease and those with impairment of hepatic function.

• Hepatic disease. In patients with acute and active hepatitis, protein binding of glucocorticoids is reduced and peak concentrations of administered glucocorticoids increased; elimination of prednisolone will also be impaired. There is an enhanced effect of corticosteroids in patients with cirrhosis.

• Epilepsy and/or seizure disorders.

• Osteoporosis: This is of special importance in post-menopausal females who are at particular risk.

• Menopausal or post-menopausal women: corticosteroid requirements may be reduced.

• Patients with existing or previous history of severe affective disorders and particularly those with a previous history of corticosteroid induced psychoses.

• Emotional instability or psychotic tendencies; these may be aggravated by corticosteroids including prednisolone.

• Cushing's Disease; glucocorticoids can produce or aggravate Cushing's Syndrome.

• Peptic ulceration.

• Previous steroid myopathy.

• Renal insufficiency.

• Ocular herpes simplex infection because of possible perforation.

• Recent myocardial infarction (rupture).

• Myasthenia gravis; glucocorticoids should be used carefully in patients receiving anticholinesterase therapy.

• Thromboembolic disorders; corticosteroids should be used with caution since cortisone has been reported rarely to increase blood coagulability and to precipitate intravascular thrombosis, thromboembolism and thrombophlebitis.

• Duchene's muscular dystrophy; transient rhabdomyolysis and myoglobinuria may occur following strenuous physical activity. It is not known whether this is due to prednisolone itself or the increased physical activity.

• Phaeochromocytoma. Glucocorticoids should be avoided or administered with caution in patients previously diagnosed with or currently under investigation for possible phaeochromocytoma. Phaeochromocytoma should be recalled as a differential diagnosis whenever patients take a sudden turn for the worse, or have acute uncontrollable hypertension following steroid administration.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos, or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves.

Establishment of secondary fungal and viral infections of the eye may also be enhanced in patients receiving glucocorticoids.

Raised intracranial pressure with papilloedema (pseudotumour cerebri) associated with corticosteroid treatment has been reported in both children and adults. The onset usually occurs after treatment withdrawal (See section 4.8).

Inflammatory bowel disease: These tablets are not enteric coated. Symptoms recurred in a patient with Crohn's Disease on changing from non-enteric coated to enteric coated tablets of prednisolone. This was not an isolated occurrence in the author's unit, and it was advocated that only non-enteric coated prednisolone tablets should be used in Crohn's disease, and that the enteric coated form should be used with caution in any condition characterised by diarrhoea or a rapid transit.

• The effect of corticosteroids may be enhanced in patients with hypothyroidism in those with chronic liver disease with impaired hepatic function.

• 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, being tapered off over weeks or months according to the dose and duration of treatment.

Prednisolone treatment is likely to reduce the response of the pituitary-adrenal axis o stress and relative adrenal insufficiency may persist for up to a year after discontinuation of therapy.

Therapy may need to be reintroduced during a period of stress.

Prolonged use of corticosteroids may result in the disturbance of electrolyte balance which is manifest in oedema, hypertension, and hypokalaemic alkalosis and in extreme cases, cardiac failure may be induced.

Use in Children

Corticosteroids cause dose-related 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 hypothalamopituitary adrenal axis and growth retardation. The growth and development of infants and children should be closely monitored. Treatment should administered where possible as a single dose on alternate days.

Use in the elderly

The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

Prednisolone withdrawal (see section 4.2)

4.5 Interaction with other medicinal products and other forms of interaction

- Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.
- Antacids can reduce the absorbtion of prednisolone if given in high doses.Indigestion remedies should not be taken at the same time of day as Prednisolone.

- Rifampicin, rifabutin, carbamazepine, phenobarbitone and other Barbiturates, carbimazole, phenylbutazone, phenytoin, primidone 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.
- 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.
- Corticosteroids may antagonise the effects of neuromuscular-blocking agents, such as pancuronium or vecuronium. Careful monitoring is needed when neuromuscular blocking agents are used in patients who have been treated with corticosteroids. An increase in the dose of the neuromuscular blocker may be required.
- 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 and beta-2-agonists, theophylline, carbenoxolone are enchanced.
- 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.
- Plasma concentration of prednisolone possibly increased by ritonavir.
- NSAIDs such as indometacin may increase the risk of GI ulceration. The possiblity of GI ulceration should be considered with concomitant use with any other NSAIDs.

- Aspirin should be used cautiously in conjunction with glucocorticoids in patients with hypoprothrombinaemia. Concurrent use of aspirin and prednisolone may result in an increased risk of gastrointestinal ulceration and subtherapeutic aspirin serum concentrations. 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.
- Antifungals: Increased risk of hypokalaemia with amphotericin. Avoid concomitant use unless corticosteroids needed to control reactions. Ketoconazole (drug that inhibit hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4) 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 haematological 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 retinoids and tetracyclines due to increased intracranial pressure.
- Oestrogens and progestogens increase plasma concentrations of corticosteroids.
- Oral contraceptives increased prednisolone concentrations by 131%. May increase AUC and reduce clearance in oral contraceptives containing ethinylestradiol, mestranol, desogestrel, levonorgestrel, norgestrel or norethisterone.
- Tumorigenicity: direct tumour-inducing effects of the glucocorticoids are not known, but the particular risk that malignancies in patients undergoing immunosupression with these or other drugs will spread more rapidly is a wellrecognised problem.
- Glycyrrhizin can delay the clearance of prednisolone.
- Growth promoting effect may be inhibited with concomitant use of prednisolone with somatropin
- Increased risk of hypokalaemia if high doses of corticosteroids given with high doses of bambuterol, fenoteral, formoterol, ritodrine, salbutamol, salmeterol and terbutaline (sympathomimetics).

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 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 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.

Lactation

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 doses of up to 40 mg daily of prednisolone are unlikely to cause systemic effects in the infants. 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

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.

Endocrine disorders

Not known: Suppression of the hypothalamic-pituitary-adrenal axis, growth suppression in infancy, childhood and adolescence. Cushingoid facies, hirsutism, impaired carbohydrate tolerance with increased requirement for anti-diabetic therapy manifestation of latent diabetes mellitus.

Infections and infestations

Not known: Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see section 4.4).

Blood and lymphatic system disorders

Not known: Leucocytosis. Increase in blood coagulability

Immune system disorders

Not known: Hypersensitivity including anaphylaxis.

Musculoskeletal and connective tissue disorders

Not known: Osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, tendinopathies, myalgia, growth suppression in infancy, childhood and adolescence. Proximal myopathy, muscle weakness, wasting and loss of muscle mass.

Metabolism and nutrition disorders:

Not known: Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis, nocturia, risk of congestive heart failure in susceptible patients. Negative protein and calcium balance, increased appetite, glucose intolerance and protein catabolism. Increase both high and low density lipoprotein cholesterol concentration in the blood. Weight gain, obesity, hyperglycaemia, dyslipidaemia.

Psychiatric disorders

Common: 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, nervousness, 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.

Not known: euphoria, psychological dependence, depression

Nervous system disorders

Not known: insomnia, dizziness, headache, vertigo. intracranial hypertension in children, aggravation of schizophrenia, Increased intra-cranial pressure with

papilloedema in children (pseudotumour cerebri), usually after treatment withdrawal. Aggravation of epilepsy, epidural lipomatosis. vertebrobasilar stroke (exacerbation of giant cell arteritis, with clinical signs of evolving stroke has been attributed to prednisolone).

Eye disorders

Not known: Increased intra-ocular pressure, glaucoma, papilloedema, posterior

subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease, scleral perforation, nuclear cataracts (particular in children), exophthalmos.

Severe exacerbation of bullous exudative retinal detachment; lasting visual loss in some patients with idiopathic central serious chorioretinopathy (see section 4.4).

Gastrointestinal disorders

Not known: Dyspepsia, peptic ulceration with perforation and haemorrhage, oesophageal ulceration, abdominal pain, diarrhoea, abdominal distension and nausea, acute pancreatitis, oesophageal candidiasis, perforation of the small bowel, particularly in patients with inflammatory bowel disease.

Skin and subcutaneous tissue disorders

Not known: Impaired healing, skin atrophy, bruising, telangiectasia, striae, acne, increased sweating, pruritis, rash, urticaria.

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 (with high dose therapy).

Vascular disorders

Not known: Thromboembolism

Reproductive system and breast disorders

Not known: Menstrual irregularity, amenorrhoea.

General disorders and administration site conditions

Not known: Malaise, fatigue and the suppression of delayed hypersensitivity reaction.

Withdrawal symptoms and signs

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 and loss of weight.

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.

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.

4.9 Overdose

Treatment is supportive and symptomatic. Serum electrolytes should be monitored.

Reports of acute toxicity are rare. There is no specific antidote and treatment is supportive and symptomatic.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC CODE: H02A B06

Prednisolone is a corticosteroid. The effects of corticosteroids are numerous and widespread. They influence carbohydrate, protein and lipid metabolism, electrolyte and water imbalance, and the functions of the cardiovascular system, the kidney, skeletal muscle, the nervous system and other organs and tissues. Furthermore, the corticosteroids endow the organism with the capacity to resist many types of noxious stimuli and environmental change.

5.2 Pharmacokinetic properties

Corticosteroids are absorbed from the gastrointestinal tract. In the circulation they are extensively bound to plasma proteins, mainly to globulin and less so to albumin. The corticosteroid-binding globulin has high affinity but low binding capacity, while the albumin has low affinity but large binding capacity. Only unbound corticosteroid has pharmacological effects or is metabolised. The synthetic corticosteroids are less extensively protein bound than hydrocortisone. They also tend to have longer half-lives.

Its initial absorption, but not its overall bioavailability, is affected by food, hepatic or renal impairment and certain drugs.

Corticosteroids are metabolised mainly in the liver but also in the kidney and are excreted in the urine. The slower metabolism of the synthetic corticosteroids with their lower protein binding affinity may account for their increased potency compared with the natural corticosteroids.

5.3. Preclinical safety data

Not available.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose monohydrate, maize starch, colloidal anhydrous silica, sodium starch glycollate, stearic acid, magnesium stearate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Do not store above 30°C. Protect from light.

6.5 Nature and contents of container

Polypropylene tubes fitted with polyethylene caps.

Pack sizes: 28, 56, 84, 100, 250, 500, and 1000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. MARKETING AUTHORISATION HOLDER

Pharmvit Limited
Unit 13, Metropolitan Trading Centre
Derby Road
Greenford
Middlesex UB6 8UJ
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 04556/0052

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 September 2003

Date of latest renewal: 09 October 2008

10 DATE OF REVISION OF THE TEXT

21/12/2017