

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Prednisolone 5 mg Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg prednisolone.

Excipient(s) with known effect:

Lactose monohydrate 71.3 mg.

For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Tablet

White, round tablet with a cross-shaped breaking notch and imprint "5" on one side.

The breakline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

## 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), autoimmune 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 and 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.

**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, Behcets disease, immunosuppression in organ transplantation.

## 4.2 Posology and method of administration

The initial dosage of prednisolone may vary from 5 mg to 60 mg daily depending on the disorder being treated. Divided daily dosage is usually used. 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 also 'Special warnings and precautions for use'*).

In patients who have received more than the physiological dose for systemic corticosteroids (approximately 7.5 mg prednisolone or equivalent) for greater than three 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 7.5 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 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 three 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 40 mg daily of prednisolone (or equivalent).
- Patients repeatedly taking doses in the evening (*see 'Special warnings and precautions for use' and 'Undesirable effects'*).

During prolonged therapy, dosage may need to be temporarily increased during periods of stress or during exacerbations of the disease (See '*Special warnings and precautions for use*').

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

***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 5-7.5 mg daily during chronic treatment.

***Allergic and Skin Disorders:*** Initial doses of 5-15 mg daily are commonly adequate.

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

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

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

***Use in Children:*** Although appropriate fractions of the actual dose may be used, dosage will usually be determined by clinical response as in adults (see also '*Special warnings and precautions for use*'). Alternate day dosage is preferable where possible.

***Use in 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 also '*Special warnings and precautions for use*').

***Method of administration:*** Oral

### 4.3 Contraindications

Systemic infections unless specific anti-infective therapy is employed. Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Peptic ulceration. Ocular herpes simplex because of possible perforation.

### 4.4 Special warnings and precautions for use

#### **A patient information leaflet should be supplied with this product.**

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 on alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity (see '*Posology and method of administration*').

Caution is necessary when oral corticosteroids, including Prednisolone Tablets, are prescribed in patients with the following conditions. Frequent patient monitoring is necessary.

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 Interactions*), 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 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.

Tuberculosis: Those with a previous history of, or X-ray changes characteristic of, tuberculosis. The emergence of active tuberculosis can, however be prevented by the prophylactic use of antituberculosis therapy.

Hypertension.

Congestive heart failure.

Liver failure.

Renal insufficiency.

Diabetes mellitus or in those with a family history of diabetes.

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

Glaucoma or in those with a family history of glaucoma.

Patients with a history of severe affective disorders and particularly those with a previous history of steroid induced psychoses.

Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids including prednisolone.

Epilepsy and/or seizure disorders.

Peptic ulceration.

Previous steroid myopathy.

Glucocorticoids should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy.

Co-treatment with CYP3A4 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 risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects (see section 4.5).

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.

#### *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 minimised 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 reinstated. Since mineralcorticoid secretion may be impaired, salt and/or a mineral-corticoid should be administered concurrently. 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.

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 duration of therapy.

#### *Anti-inflammatory/Immunosuppressive effects and Infection:*

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 infection such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised when corticosteroids such as prednisolone are used. 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 specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased. The effect of corticosteroids may be enhanced in patients with hypothyroidism and in those with chronic liver disease with impaired hepatic function.

#### *Measles:*

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

#### *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 3 months after stopping corticosteroid therapy. (See also *section 4.5 'Interactions'*).

#### *Ocular Effects:*

Prolonged use of corticosteroids may produce posterior subcapsular and nuclear cataracts (particularly in children), exophthalmos, or increased intraocular pressure, which may result in glaucoma with possible damage to optic nerves. Establishment of secondary fungal and viral infections of the eye may also be enhanced in patients receiving glucocorticoids.

#### *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.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible perforation.

*Cushing's Disease:*

Because glucocorticoids can produce or aggravate Cushing's syndrome, glucocorticoids should be avoided in patients with Cushing's disease.

Psychic derangements may appear when corticosteroids, including prednisolone, are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations.

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

*Paediatric population:*

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 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.

As the medicine contains lactose monohydrate 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

**Hepatic microsomal enzyme inducers:** Drugs which can cause liver enzyme induction 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 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. Co-treatment with CYP3A4 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 risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

**Antidiabetic agents:** Glucocorticoids may increase blood glucose levels. Patients with diabetes mellitus receiving concurrent insulin and/or oral hypoglycaemic agents may require dosage adjustments of such therapy.

**Non-steroidal anti-inflammatory drugs:** Concomitant administration of ulcerogenic drugs such as indometacin 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 hyperkalaemia 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 hyperkalaemia if high doses of corticosteroids given with high doses of bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline.

**Other:** The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids and the hypokalaemic effect of acetazolamide, loop diuretics, thiazide diuretics, carbenoxolone and theophylline are enhanced.

## 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. 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.

#### 4.7 Effects on ability to drive and use machines

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

#### 4.8 Undesirable effects

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.

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 '*Special warnings and precautions for use*').

**Body as a Whole:** Leucocytosis, hypersensitivity including anaphylaxis, thromboembolism, fatigue, malaise.

**Cardiovascular:** Congestive heart failure in susceptible patients, hypertension.

**Gastrointestinal:** Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis.

**Musculo-skeletal:** Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, myalgia.

**Metabolic/ Nutritional:** Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen and calcium balance.

**Dermatological:** Impaired healing, hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, may suppress reactions to skin tests, pruritis, rash, urticaria.

**Endocrine/Metabolic:** Suppression of the hypothalamo-pituitary adrenal axis particularly in times of stress as in trauma, surgery or illness, growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea, Cushingoid facies, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of diabetes mellitus, increased appetite.

**Central and Peripheral Nervous System:** Euphoria, psychological dependence, depression, insomnia, dizziness, headache, vertigo. Raised intracranial pressure with papilloedema (pseudotumor cerebri) in children, usually after treatment withdrawal. Aggravation of schizophrenia. Aggravation of epilepsy.

**Ophthalmic:** Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease, central serous chorioretinopathy.

**Eye disorders:** rare: Vision, blurred (see also section 4.4)

**Scleroderma renal crisis:** Frequency 'unknown' (see also section 4.4). 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%)



**Anti-inflammatory and immunosuppressive effects:** Increases susceptibility to, and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see Special warnings and precautions for use).

**General:** Leucocytosis, hypersensitivity including anaphylaxis, thromboembolism, nausea, malaise.

**Withdrawal Symptoms:** Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see 'Special warnings and precautions for use' and 'Posology and method of administration'). A withdrawal syndrome may also occur including: fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, loss of weight, anorexia, nausea, vomiting, lethargy, headache, desquamation and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels.

#### 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

## 4.9 Overdose

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

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacodynamic Group: Corticosteroids for systematic use, plain

ATC Code: H02A

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 response to diverse stimuli.

### 5.2 Pharmacokinetic properties

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

Prednisolone shows dose dependant pharmacokinetics, with an increase in dose leading to an increase in volume of distribution and plasma clearance. The degree of plasma protein binding determines the distribution and clearance 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.

### **5.3 Preclinical safety data**

No further information provided.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Lactose monohydrate  
Potato starch  
Colloidal anhydrous silica  
Sodium starch glycolate (Type A)  
Magnesium stearate

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

4 years.

### **6.4 Special precautions for storage**

Do not store above 25°C. Store in the original container package in order to protect from moisture. Keep blister in the outer package in order to protect from light.

### **6.5 Nature and contents of container**

PVC/PVdC/Aluminium blisters.

28, 30, 56, 60, 98, 100, 140 & 150 tablets.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements.

## **7 MARKETING AUTHORISATION HOLDER**

Clonmel Healthcare Limited  
Waterford Road  
Clonmel  
County Tipperary  
Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA0126/027/001

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 01 September 1982

Date of last renewal: 02 June 2007

**10 DATE OF REVISION OF THE TEXT**

November 2017