Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Prednisolone 5 mg soluble tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soluble tablet contains 5 mg prednisolone as prednisolone sodium phosphate

Excipient(s) with known effect
Each tablet contains 27.9 mg sodium and 7.5 mg sodium benzoate.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soluble Tablet
Pink, round, marked with 'PD' on one side and scored with a break-line on the other side. The tablet size is 7.00 mm. The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A wide variety of diseases may sometimes require corticosteroid therapy.

Prednisolone is used principally for its anti-inflammatory and immunosuppressant action or anti-neoplastic properties.

Prednisolone may also be used as a replacement therapy but cortisone is usually preferred.

The major indications are listed below. This list of indications is not exhaustive but represents the major established disease states with evidence of an established and current role in their management.
Prednisolone may be used in a wide variety of other inflammatory and immune disorders according to local guidelines and according to the assessment of the benefit risk in individual patients.

Inflammatory and immunological disorders

- Pemphigus
- Sarcoid disease

Respiratory disorders

- Asthma

Rheumatic disorders

- Rheumatoid arthritis, polymyalgia rheumatica and giant cell (temporal) arteritis and polyarteritis nodosa

Collagen diseases and connective tissue disorders

- Systemic lupus erythematosus,
- Polymyositis

Gastrointestinal disorders

- Inflammatory bowel disease: ulcerative colitis and Crohn's disease
- Autoimmune hepatitis

Renal disorders

- minimal change nephrotic syndrome, acute interstitial nephritis; renal lupus

Blood disorders

- Thrombocytopenic purpura and acquired haemolytic anaemia

Immunological disorders

- Immunosuppression – in organ transplantation

Neoplasms Treated with Corticosteroids
Prednisolone is an established component of chemotherapeutic regimes used in the treatment of the following neoplasms:

- Acute Lymphoblastic Leukemia (including the acute blastic phase of myeloid leukaemia resembling acute lymphoblastic leukemia)
- Chronic Lymphocytic Leukemia
- Hodgkin Lymphoma
- Non-Hodgkin Lymphoma

4.2 Posology and method of administration

Posology
The lowest dosage that will produce an acceptable result should be used. When it is possible to reduce the dose this should be done in stages. During prolonged therapy, dosage may need to be increased temporarily during periods of stress or in exacerbations of illness.

Adults:
The dose used will depend upon the disease, its severity and the clinical response obtained. The following regimens are for guidance only. Local guidance should be taken into consideration. Divided dosage is usually employed.

Short-term treatment:
20 to 30mg daily for the first few days, subsequently reducing the daily dosage by 2.5 or 5mg every two to five days, depending upon the response.

Rheumatoid arthritis:
7.5 to 10mg daily. For maintenance therapy the lowest effective dosage is used.

Most other conditions:
10 to 100mg daily for one to three weeks, then reducing to the minimum effective dosage.

Paediatric population:
Fractions of the adult dosage may be used (e.g. 75% at 12 years, 50% at 7 years and 25% at 1 year) but clinical factors must be given due weight. Local guidance should be taken into consideration.

Prednisolone Soluble Tablets may be given early in the treatment of acute asthma attacks in children. For children over 5 years use a dose of 30-40mg prednisolone.

For children aged 2-5 years use a dose of 20mg prednisolone. Those already receiving maintenance steroid tablets should receive 2mg/kg prednisolone up to a maximum dose of 60mg. The dose of prednisolone may be repeated for children who vomit; but intravenous steroids should be considered in children who are unable to retain orally ingested medication. Treatment for up to three days is usually sufficient, but the length of course should be tailored to the number of days necessary to bring about recovery. There is no need to taper the dose at the end of treatment.

For children under 2 years, Prednisolone Soluble Tablets can be used early in the management of moderate to severe episodes of acute asthma in the hospital setting, at a dose of 10mg for up to three days.

Growth retardation in children
To try to minimize growth retardation in children, corticosteroid therapy should be prescribed on alternate days (one day without corticosteroids followed by a day with twice the usual daily dose). This alternate-day regimen can only be considered once control of the inflammatory disease has been established with high corticosteroid doses and on condition that no rebound is observed when the dose is reduced.

Method of administration:
For oral use only

Prednisolone Soluble Tablets are best taken dissolved in water, but they can be swallowed whole without difficulty. When dissolved in water the resulting solution must be drunk immediately by the patient.

Drug withdrawal following prednisolone treatment for three weeks or longer should not be abrupt to avoid relapse of disease. Once a daily dose equivalent to 7.5 mg prednisolone is reached, dose reduction must be slow to allow the hypothalamic-pituitary-adrenal (HPA) axis to recover (See Section 4.4).

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Use in patients with peptic ulcer, active tuberculosis, acute psychosis, acute bacterial or viral infections (including chicken-pox and shingles) unless specific anti-infective or anti-ulcer therapy is employed.
- Live virus immunization and use in patients who have recently been immunised (see section 4.5 Interaction with other medicinal products and other forms of interaction).

4.4 Special warnings and precautions for use

Adrenal cortical atrophy and withdrawal symptoms
Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. 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. 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. Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight. In some instances, withdrawal symptoms may involve or resemble a clinical relapse of the disease for which the patient has been undergoing treatment. Other effects that may occur during withdrawal or change of corticosteroid therapy include benign intracranial hypertension with headache and vomiting and papilloedema caused by cerebral oedema. Latent rhinitis or eczema may be unmasked.

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 7.5 mg prednisolone is reached, dose reduction should be slower to allow the HPA axis to recover.

Abrupt withdrawal of systemic corticosteroid treatment, which has continued for no longer than 3 weeks, is appropriate if it is considered that the disease is unlikely to relapse. However gradual withdrawal of systemic corticosteroid therapy is appropriate even after courses lasting less than 3 weeks if any of the following applies:

- 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.
- 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 any intercurrent illness, trauma or surgical procedure may require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy they may need to be temporarily re-introduced.

Suppression of the HPA axis and other 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 alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity. (See dosage section). 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.

Increased susceptibility to infections including risk of chicken pox or tuberculosis, and risks associated with use of live vaccines
Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The resultant opportunistic infections may be fatal. 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.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients 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 medical attention. If the patient is a child parents must be given the above advice. 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.

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

Live vaccines should not be given to individuals with impaired immune responsiveness caused by high doses of corticosteroids. The antibody response to other vaccines may be diminished.

Corticosteroids should be given with care in patients with a history of tuberculosis or the characteristic appearance of tuberculosis disease on X-Ray. If corticosteroids are indicated in patients with latent tuberculosis or in tuberculin-reactive patients, these patients must be monitored carefully as recurrence of the disease may occur. In the event of long-term corticosteroid treatment, patients should receive prophylactic anti-tuberculosis treatment. If rifampicin is used in anti-tuberculosis programmes, consideration must be given to the increased effect of rifampicin on the metabolic clearance of corticosteroids in the liver. It may therefore be necessary to increase the dose of corticosteroid.

Corticosteroid therapy can promote the onset of various infectious complications caused, in particular, by bacteria, yeasts and parasites. The onset of 'malignant' strongyloidiasis is a major risk. All patients having travelled from an endemic region (tropical or subtropical regions, southern Europe) should have parasitological stool tests and receive systematic eradication treatment before corticosteroid treatment.

Any potential visceral foci should be ruled out prior to treatment initiation and patients monitored for possible onset of infection during treatment.

Immunosuppression and cancer risk
Chronic immunosuppression (e.g. in the setting of organ transplantation), has been associated with an increased risk of malignancy.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.

Psychiatric reactions, sometimes severe, particularly in patients with a history of affective disorders

Psychiatric and behavioural problems. 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 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. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected.

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.

Endocrine and metabolic changes
The following principal endocrine and metabolic changes occur when higher doses of prednisolone (generally more than 7.5 mg daily in adults) are given for prolonged periods:

- cushingoid facies, with skin thinning hirsutism fluid retention and weight gain
- decreased carbohydrate tolerance, particularly in diabetic patients.
- osteoporosis, particularly post-menopausal women

As a result of these effects care and frequent patient monitoring is necessary in patients with the following complaints: diabetes mellitus (or a family history of diabetes), osteoporosis (post-menopausal women are particularly at risk), hypertension, congestive heart failure (because of the possibility of fluid retention), patients with a history of severe or pre-existing affective disorders (especially a history of steroid psychosis), glaucoma or a family history of glaucoma, previous corticosteroid induced myopathy, epilepsy, liver failure, renal insufficiency or with a history of peptic ulceration (see section 4.8 'Undesirable effects'). Prednisolone is contra-indicated in active peptic ulceration (see section 4.3 Contraindications) unless specific anti-ulcer therapy is employed. In patients with a history of ulcer, corticosteroid therapy may be prescribed, under clinical monitoring and, if necessary, after fibroscopy. Impaired wound healing may also occur.

Oral or injectable corticosteroids may promote the development of tendon injuries or even tendon rupture (in exceptional cases). This risk is increased in the event of co-administration with fluoroquinolones and in dialyzed patients with secondary hyperparathyroidism or who have undergone renal transplantation.

This medicinal product is not recommended in combination with acetylsalicylic acid at anti-inflammatory doses (see section 4.5).

Athletes are warned that this medicinal product contains an active substance that may produce a positive result in anti-doping tests.

The development of pheochromocytoma crises, which can be fatal, has been reported after administration of corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation (see section 4.8).

Visual disturbance
Visual disturbance may develop in patients receiving systemic or topical corticosteroid therapy. If patients experience blurred vision or other visual disturbances during corticosteroid therapy, an ophthalmological examination is required to investigate, in particular, the possible presence of a cataract, glaucoma or a rarer condition such as central serous chorioretinopathy (CSCR), reported with the administration of systemic or topical corticosteroids.

Fluid retention Because of the possibility of fluid retention, care must be taken when corticosteroids are administered to patients with renal insufficiency or hypertension or congestive heart failure. Medium or high doses of hydrocortisone and cortisone may in fact cause an increase in blood pressure, water-electrolyte retention and increased excretion of potassium. These effects are less possible with a usage of synthetic derivatives except when used in high doses. Dietary salt restrictions and potassium supplementation may be required. All the corticosteroids increase a calcium excretion

Paediatric population:

Growth retardation in children. Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. In order to minimize suppression of the HPA axis and growth retardation treatment should be limited to the minimum dosage for the shortest possible time, and consideration should be given to administration of a single dose on alternate days.

Special Populations
The use of corticosteroids requires particularly specific monitoring, especially in the elderly and in those with ulcerative colitis (risk of perforation), recent intestinal anastomoses, renal failure, liver failure, osteoporosis and myasthenia gravis.

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.

Patients with renal impairment
Because of the possibility of fluid retention, care must be taken when corticosteroids are administered to patients with renal insufficiency. There is significant renal elimination of prednisolone and its metabolites so that reduced dosing may be appropriate in patients with impairment of renal function. There are no specific recommendations for dosage adjustment in patients with renal failure.

Patients with hepatic impairment:
Prednisolone undergoes extensive hepatic metabolism and plasma levels are known to be increased in hepatic disease so that reduced dosing may be appropriate in patients with hepatic impairment.

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.

Excipients:
This medicinal product contains 27.9 mg sodium per tablet, equivalent to 1.4 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicine contains 7.5 mg benzoate salt in each tablet which can cause an increase in bilirubinaemia following its displacement from albumin This may increase neonatal jaundice which may develop into kernicterus (non-conjugated bilirubin deposits in the brain tissue).

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacokinetic Interactions
Increased effect of prednisolone
Ciclosporin increases plasma concentration of prednisolone. A similar increase in plasma concentration of prednisolone may also occur with ritonavir.
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.

Reduced Effect of Prednisolone
The therapeutic effect of steroids may be reduced by phenytoin, phenobarbitone, ephedrine, rifabutin, primidone aminoglutethimide, carbamazepine and rifampicin, as they all enhance the metabolism of corticosteroids. Mifepristone may reduce the effect of corticosteroids for 3-4 days.

Increased efficacy of other drugs
The efficacy of coumarin anticoagulants and warfarin may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding. The dosage of concomitantly administered anti-coagulants may have to be altered (usually decreased).

Pharmacodynamic Interaction.

Increased Effect of Prednisolone
Oestrogens and other oral contraceptives may potentiate the effects of glucocorticoids and dosage adjustments may be required if oestrogens are added to or withdrawn from a stable dosage regimen.

Increased Effect of other treatment
Concomitant use of aspirin and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) with corticosteroids increases the risk of gastro-intestinal bleeding and ulceration.
The hypokalaemic effects of acetazolamide, loop diuretics such as furosemide, thiazide diuretics such as bendroflumethiazide, and carbenoxolone, theophylline and amphotericin are enhanced by corticosteroids.

Potassium-depleting agents
Hypokalemia is a factor promoting the onset of cardiac arrhythmias (in particular, torsades de pointes) and increasing the toxicity of certain medicinal products, such as digoxin. Consequently, medicinal products that may induce hypokalemia are implicated in numerous interactions. These include potassium-depleting diuretics, alone or in combination, stimulant laxatives, glucocorticoids, tetracosactide and amphotericin B (IV route).

Digoxin
Hypokalemia promotes the toxic effects of digitalis drugs. Any hypokalemia should be corrected beforehand and clinical, electrolyte and ECG monitoring performed.
Medicinal products likely to induce torsades de pointes
There is an increased risk of ventricular arrhythmias, especially torsades de pointes. Any existing hypokalemia should be corrected before administration, and clinical, electrolyte and ECG monitoring performed.

Corticosteroids should not be given concomitantly with amphotericin, unless required to control reactions. The risk of hypokalaemia also increases if high doses of corticosteroids are given with high doses of bambuterol, fenoterol, formoterol, salbutamol, salmeterol and terbutaline. The toxicity of cardiac glycosides is increased if hypokalaemia occurs with corticosteroids.

Concomitant use with methotrexate may increase the risk of haematological toxicity.

Fluoroquinolones
The risk of tendon disease, or even tendon rupture (in exceptional cases) may increase, particularly in patients receiving long-term corticosteroid therapy.

Reduced Effect of other drugs
The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids.
The growth promoting effect of somatotropin may be inhibited by the concomitant use of corticosteroids. Steroids may reduce the effects of anticholinesterases in myasthenia gravis and cholecystographic x-ray media.
The renal clearance of salicylates is increased by corticosteroids. However in the case of steroid withdrawal there may be a risk of salicylate toxicity.
Isoniazid plasma concentrations are decreased due to increased hepatic metabolism of isoniazid and reduced hepatic metabolism of glucocorticoids. Clinical and laboratory monitoring are required.

Effects on live and inactivated virus vaccines.
Prednisolone, particularly in immunosuppressive doses, reduces the response to virus infections. Live vaccines can, in some situations, cause severe or fatal infections in immunosuppressed individuals due to extensive replication of the vaccine strain.

Live virus vaccines should not be administered to patients on immune-suppressant doses of corticosteroids (see 4.4 Special precautions and warnings).

If inactivated vaccines are administered to patients being treated with prednisolone the expected serum antibody response may not be obtained (see 4.4 Special precautions and warnings).

4.6 Fertility, pregnancy and lactation

Pregnancy
The ability of corticosteroids to cross 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 intrauterine 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. A period of clinical (weight, urine output) and laboratory monitoring of the newborn is justified.
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. Depression of hormone levels has been described in pregnancy but the significance of this finding is not clear.

Breast-feeding
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.
However, breast-feeding is not recommended in the event of chronic treatment with high doses.

4.7 Effects on ability to drive and use machines

The effect of Prednisolone soluble tablets on the ability to drive or use machinery has not been evaluated. As psychiatric and behavioural problems may occur especially when higher doses are taken patients should be advised to avoid driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected.

4.8 Undesirable effects

Undesirable effects listed in the table are grouped by MedDRA System Organ Classes and are ranked under heading of frequency, using the following convention, when applicable: very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1000); very rare (<1/10, 000); not known (cannot be estimated from the available data).

Corticosteroid administration will result in certain effects, the severity, significance and extent of which vary with the dosage and duration of treatment and the particular corticosteroid used. While some reactions are clearly common and others are known to be rare the frequency of many reactions is impossible to characterize and is given as unknown.

System organ class	Undesirable effects	Frequency
Infections and infestations	Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see section 4.4).	Not known
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission. Pheochromocytoma crises, cases of tumor lysis syndrome have been reported in patients with hematological malignancies (see section 4.4)	Not known
Blood and lymphatic system disorders	Diminished lymphoid tissue and immune response; increase in blood coagulability. Leukocytosis.	Not known
Immune system disorders	Hypersensitivity including anaphylaxis has been reported.	Not known
Endocrine disorders	Inhibition of pituitary function which is dose and time dependent. Cushingoid Syndrome; features of hypercorticolism, such as suppression of the HPA axis. Impaired carbohydrate intolerance with increased requirement for anti-diabetic therapy; manifestation of latent diabetes mellitus; hypokalaemic alkalosis.	Not known
Metabolism and nutrition disorders	Fluid retention (see section 4.4 'Special warnings and precautions for use'); disturbance in electrolyte imbalance,	Not known

	glucose metabolism, mineral metabolism and gluconeogenesis, diabetes mellitus	
Psychiatric disorders	A wide range of psychiatric reactions including affective disorders such as irritability, euphoria, depressed and labile mood, and suicidal thoughts; psychotic reactions including mania, delusions, hallucinations, and aggravation of schizophrenia; behavioural disturbances; irritability; anxiety; sleep disturbances; cognitive dysfunction including confusion and amnesia. Reactions may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%.	Common
Nervous system disorders	Dizziness, headache Benign intracranial hypertension Increased intracranial pressure with papilloedema in children (pseudotumour cerebri) - usually after treatment withdrawal. Epilepsy - aggravation of epilepsy.	Not known Rare Rare Not known
Eye disorders	Glaucoma, papilloedema, posterior subcapsular cataracts, central serous chorioretinopathy, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases.	Not known
Ear and labyrinth disorders	Vertigo	Not known
Cardiac disorders	Myocardial rupture following recent myocardial infarction. Congestive cardiac failure (in susceptible patients). Bradycardia*	Not known
Vascular disorders	Hypertension, thrombo-embolism.	Not Known
Respiratory, thoracic and mediastinal disorders	Hiccups.	Not Known
Gastrointestinal disorders	Peptic ulceration or its aggravation; with perforation and haemorrhage. Dyspepsia, nausea, vomiting, abdominal distension, abdominal pain, diarrhoea, oesophageal ulceration, candidiasis, pancreatitis acute.	Not Known
Skin and subcutaneous tissue disorders	Skin Atrophy, skin striae, acne, telangiectasia, hyperhidrosis, rash, pruritus, urticaria, hirsutism.	Not Known
Musculoskeletal and connective tissue disorders	Osteoporosis, aseptic osteonecrosis particularly of femoral head; vertebral and long bone fractures, Myopathy and myalgia Growth retardation in infancy, childhood and adolescence.	Not Known
Reproductive system and breast disorders	Menstruation irregular, amenorrhoea.	Not Known
Renal and urinary disorders	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%)	Not Known
General disorders and administration site conditions	Impaired healing, malaise.	Not known
Investigations	Nitrogen depletion Weight increased. Hypokalaemia	Not known
Injury, poisoning and procedural complications	Tendon rupture, contusion (bruising).	Not known
Withdrawal Symptoms	Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A 'withdrawal	Not known

	syndrome' may also occur (See Section 4.4) including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.	

*Following high doses

Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

Hypersensitivity including anaphylaxis has been reported after long-term systemic use of corticosteroids.

In patients with liver failure blood levels of corticosteroid may be increased, as with other drugs which are metabolized by the liver.

*Aseptic osteonecrosis, particularly of the femoral head, may occur after prolonged corticosteroid therapy or after repeated short courses involving high dosage.

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 Website: www.hpra.ie.

4.9 Overdose

Acute over dosage requiring treatment is unlikely to occur and only supportive and symptomatic therapy is indicated. However in the case of chronic intentional or unintentional over dosage, misuse or abuse the features of hypercortisolism may appear and in this situation the product should be discontinued slowly.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glucocorticoids

ATC code: H02AB06

Prednisolone sodium phosphate is a synthetic glucocorticoid with the same general properties as prednisolone itself and other compounds classified as corticosteroids. Prednisolone is four times as active as hydrocortisone on a weight for weight basis.

Prednisolone irreversibly binds with glucocorticoid receptors found in virtually all tissues so that prednisolone can activate and influence biochemical behaviour of most cells. The steroid/receptor complexes interact with cellular DNA in the nucleus, binding to steroid-response elements and modifying gene transcription. They both induce synthesis of some genes and, therefore, some proteins, and inhibit synthesis of others. Not all metabolic actions on genes are known.

Inhibition of gene transcription for COX-2, cytokines, cell adhesion molecules, and inducible NO synthetase occurs ant there is blockage of the vitamin D3-mediated induction of osteocalcin gene in osteoblasts and modification of collegenase gene transcription. These pharmacodynamic actions give rise to the clinical effects of suppression of inflammation and immune response and also to adverse effects such as changes in glucose homeostasis, proteolysis and lipolysis.

Prednisolone sodium phosphate is very soluble in water, and is therefore less likely to cause local gastric irritation than prednisolone, which is only slightly soluble. This is important when high dosages are required, as in immunosuppressive therapy.

5.2 Pharmacokinetic properties

Absorption
Prednisolone is readily absorbed from the gastrointestinal tract with peak plasma concentrations achieved by 1-2 hours after an oral dose. Plasma prednisolone is mainly protein bound (70-90%), with binding to albumin and corticosteroid-binding globulin. The plasma half-life of prednisolone, after a single dose, is between 2.5-3.5 hours.

Distribution

The volume of distribution and clearance of total and unbound prednisolone are concentration dependent and this has been attributed to saturable protein binding over the therapeutic plasma concentration range.

Biotransformation
Prednisolone is extensively metabolised, mainly in the liver, but the metabolic pathways are not clearly defined.

Elimination
Over 90% of the prednisolone dose is excreted in the urine, with 7-30% as free prednisolone and the remainder being recovered as a variety of metabolites.

5.3 Preclinical safety data

No additional data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium acid citrate
Sodium bicarbonate
Saccharin sodium
Erythrosine
Povidone K30
Sodium benzoate (E 211)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

33 months

6.4 Special precautions for storage

Do not store above 30^{o}C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Prednisolone soluble tablets are available in Polyamide/aluminium/polyvinyl chloride-aluminium blister packs of 20, 30 and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Activase Pharmaceuticals Limited
Boumpoulinas 11
Nicosia
1060
Cyprus

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 21st March 2025

10 DATE OF REVISION OF THE TEXT