SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Prednisolone Tablets 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Prednisolone BP 5.00 mg

Excipients with known effect

Also contains lactose (66.4 mg).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet

4.1 Therapeutic indications

Allergy and anaphylaxis: Bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema, anaphylaxis, incapacitating allergies unresponsive toconventional treatment.

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

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

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

Endocrine disorders: Primary or secondary adrenocortical insufficiency, congenital adrenal hyperplasia.

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

Hypercalcaemia: sarcoidosis, vitamin D excess.

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

Muscular disorders: polymyositis, dermatomyositis.

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

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

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

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

Respiratory disease: allergic pneumonitis, asthma, occupational asthma, pulmonary aspergillosis, pulmonary fibrosis, pulmonary alveolitis, aspiration of foreign body, aspiration of stomach contents, pulmonary sarcoid, drug induced lung disease, adult respiratory distress syndrome, spasmodic croup, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculosis chemotherapy.

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

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

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

4.2 Posology and method of administration

Posology

Adults and the elderly

The lowest effective dose should be used for the minimum period.

Children

Prednisolone should only be used when specifically indicated, at the lowest dose possible and for the shortest possible time.

The initial dosage of Prednisolone may vary from 5mg to 60mg daily depending on the disorder being treated. Divided daily dosage may be used. Administration as a once daily dose in the morning or on alternate days can reduce the risk of adrenocortical suppression (see Section 4.4 Special warnings and precautions for use). In some patients this may not be possible e.g. patients with rheumatoid arthritis with pronounced morning stiffness where an evening dose may need to be given.

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

The lowest dose to produce an acceptable result should be given Initial dosage should be adjusted until the desired clinical response has been achieved. The dose should be gradually reduced until the lowest dose which will maintain an adequate clinical response is reached. As a guide, the daily dose should be reduced by 2.5 – 5 mg every second to fifth day (more rapidly at the higher initial dose levels) until the lowest possible maintenance dose is reached. Preferably this should not exceed 10 mg per day. Use of the lowest effective dose will tend to minimise side-effects. The incidence of side-effects increases with dose and duration of treatment (see Section 4.4 'Special warnings and special precautions for use').

Where prompt relief is urgent, high dosages are permissible and may be mandatory for a short time. In chronic conditions the lowest dose which provides adequate relief should be used. During periods of spontaneous remission corticosteroiods should be gradually discontinued.

Withdrawal warnings

Particular care should be exercised in patients who have received higher than 7.5 mg prednisolone daily or equivalent for more than 3 weeks, owing to a greater risk of suppression of the hypothalamic-pituitary-adrenal (HPA) axis in these patients. The speed with which dose can be reduced is also dependent on risk of relapse of the disease being treated. After prolonged treatment, tapering of dose below 7.5 mg (regarded as “equivalent” to physiological levels of glucocorticoids) should be conducted particularly cautiously.

More rapid withdrawal of systemic corticosteroid treatment that has been given for less than3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Withdrawal of doses of up to 40 mg daily of prednisolone, or equivalent have been administered for less than 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

- Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks,
- When a short course has been prescribed within one year of cessation of long-term therapy (months or years),
- Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroids therapy,
- Patients receiving doses of systemic corticosteroid greater than 40 mg daily of prednisolone (or equivalent),
- Patients repeatedly taking doses in the evening.

(See Section 4.4 'Special warnings and special precautions for use' and Section 4.8 'Undesirable effects')

During prolonged therapy, dosage may need to be temporarily increased during periods of stress or during exacerbations of the disease (see Section 4.4 'Special warnings and special precautions for use')

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

Intermittent dosage regimen

A single dose of PrednisoloneTablets 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 corticosteroidresponsive disorders are for guidance only. Acute or severe disease may require initial high dose therapy with reduction to the lowest effective maintenance dose as soon as possible. Dosage reductions should not exceed 5-7.5mg daily during chronic treatment.

Allergic and skin disorders

Initial doses of 5-15mg daily are commonly adequate.

Collagenosis

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

Rheumatoid arthritis

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

Blood disorders and lymphoma

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

Special populations

Use in elderly Treatment of elderly patients, particularly if long-term, should be undertaken with caution bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age (see also 'Special warnings and special precautions for use').

Use in children: Although appropriate fractions of the adult dose may be used, dosage will usually be determined by clinical response as in adults (see also Section 4.4 'Special warnings and special precautions for use' and Section 4.8 'Undesirable effects'). Alternate day dosage is preferable where possible.

Method of administration

Prednisolone tablets should be taken following a meal to reduce the risk of gastric irritation

4.3 Contraindications

i. Hypersensitivity to active substance or to any of the excipients listed in section 6.1.
ii. Systemic yeast infection
iii. Administration of live vaccines is contraindicated in patients receiving corticosteroids in immunosuppressive doses.
iv. In those conditions when treatment with prednisolone can save lives, none of the contraindications generally apply.

4.4 Special warnings and precautions for use

Since the complications of glucocorticoid therapy are dependent on the dose and duration of treatment, a risk / benefit assessment must be made in each

case regarding dose and duration of treatment, as well as whether daily or intermittent treatment should be used.

The lowest possible corticosteroid dose needed to control the disease being treated should be used. When dose reduction is possible, it should be gradual.

Immunosuppressive effects / increased susceptibility to infection

Glucocorticoids, including prednisolone, may cause increased susceptibility to infection, masking symptoms of infection, and new infections may occur during treatment.

Infections caused by viruses, bacteria, fungi, protozoa or intestinal worms may be associated with the use of corticosteroids alone or corticosteroids in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity or the function of neutrophils. The infections can be mild, but also difficult and in some cases fatal. The risk of infectious complications increases with increasing dose.

Glucocorticoids should not be given during infections without concomitant causal treatment

Chickenpox and measles can be more serious or even fatal in non-immunised children and adults treated with corticosteroids. Children, or adults who have not had these diseases, and who take immunosuppressive doses of corticosteroids, should be advised to avoid exposure to chickenpox and measles, and to seek care when exposed..

The use of prednisolone in active tuberculosis must be limited to those cases of fulminant or disseminated tuberculosis where the corticosteroid is used to treat the disease in combination with appropriate tuberculosis therapy. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close monitoring is necessary as the disease can be reactivated. In long-term corticosteroid therapy, these patients should receive tuberculosis prophylaxis.

High dose corticosteroids may interfere with active immunisation.

Vaccination with live vaccine should be done under close supervision and not in patients on long-term treatment with corticosteroids in immunosuppressive doses.

Immune system

Since rare cases of skin reactions and anaphylactic / anaphylactoid reactions have occurred in patients treated with corticosteroids, appropriate precautions should be taken prior to administration, especially if the patient has previously had an allergic reaction to any drug.

Endocrine system

Long-term treatment with pharmacological doses of corticosteroid may lead to secondary adrenal insufficiency. The risk can be reduced by giving the treatment every other day (see section 4.2).

Patients who receive corticosteroid maintenance therapy and are exposed to unusual stresses (e.g. infection, surgery or trauma) need higher corticosteroid doses before, during and after the stressful situation.

Abrupt discontinuation of treatment may lead to acute adrenal insufficiency which may be fatal. The risk of secondary adrenal insufficiency can be reduced by gradually decreasing the dose. This type of relative insufficiency may persist for months after the end of treatment, so hormone replacement therapy should be reintroduced in stressful situations occurring during this time period. Since the secretion of mineral corticoids may be impaired, salts and / or mineral corticoids should be administered simultaneously.

A "steroid withdrawal syndrome", apparently without associated with adrenal insufficiency, may also occur following abrupt withdrawal of glucocorticoids. This syndrome causes symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss and / or hypotension. These effects are believed to be due to the sudden change in glucocorticosteroid concentration rather than to low corticosteroid levels.

Patients with hypothyroidism or liver cirrhosis will have an enhanced effect of corticosteroids.

Pheochromocytoma-related crisis, which may be fatal, has been reported following systemic corticosteroid administration. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma following consideration of individual risk / benefit.

Metabolism and nutrition

Corticosteroids, including prednisolone, can raise blood sugar levels, worsen existing diabetes and increase the risk of developing diabetes in patients on long-term corticosteroid therapy.

Mental disorders

Potentially serious mental disorders may occur during treatment with corticosteroids including prednisolone. It can be anything from euphoria, sleep disorders, mood swings, personality changes and severe depression to psychotic manifestations. Existing emotional instability and psychotic tendencies can also be exacerbated by corticosteroids (see section 4.8). Symptoms typically begin within a few days or weeks after the start of treatment. Most reactions return after dose reduction or withdrawal, but specific treatment may be necessary.

Psychiatric effects have been reported with the withdrawal of corticosteroids, the frequency is unknown. Patients/carers should be encouraged to seek medical care if the patient shows mental symptoms, especially if depression or suicidal thoughts are suspected. Patients / caregivers should be aware that mental disorders may occur either during or immediately after dose reduction / discontinuation of systemic steroids.

Central and peripheral nervous system

Corticosteroids should be used with caution in patients with seizures.

Heart

Side effects of glucocorticoids on the cardiovascular system, for example dyslipidaemia and hypertension, can predispose in treated patients with existing cardiovascular risk factors for additional cardiovascular events at high doses and prolonged treatment times. Corticosteroids should therefore be introduced to these patients only after careful consideration, and risk-modifying measures as well as extra cardiac monitoring should be considered as needed. Low dose and treatment every other day can reduce the complications of corticosteroid treatment.

Blood vessels

Since cortisone has been reported to increase the blood clotting tendency in rare cases, thereby accelerating the development of intravascular thrombosis, thromboembolism and thrombophlebitis, corticosteroids should be used with caution in patients with thromboembolic disorders.

Gastrointestinal tract

High doses of corticosteroids can cause acute pancreatitis. There are no conclusive data that states that corticosteroids cause ulcers.

Glucocorticoid therapy can mask peritonitis and other signs and symptoms associated with gastrointestinal conditions such as perforation, obstruction or pancreatitis. In combination with NSAIDs, the risk of gastrointestinal ulcers is increased. Corticosteroids should therefore be used with caution in non-specific ulcerative colitis if there is a likelihood of imminent perforation, abscess or other pyogenic infection, diverticulitis, newly created anastomoses, or active or latent peptic ulcer.

Liver and biliary tract

Diseases of the liver and bile ducts have been reported rarely and in the majority of these cases the condition was reversible after discontinuation of treatment. Appropriate monitoring measures are required.

Musculoskeletal system

Acute myopathy has been reported with high corticosteroid doses, most often in patients with neuromuscular transmission disorders (e.g., myasthenia gravis), or in patients concomitantly treated with anticholinergics, e.g. neuromuscular blocking drugs (such as pancuronium) (see section 4.5). This acute myopathy is generalised, may involve eye and respiratory muscles, and may lead to tetraparesis. Elevated creatine kinase may occur. Clinical improvement or recovery after discontinuation of corticosteroid therapy may take weeks or years.

Corticosteroids should be used with caution in patients with osteoporosis.

Kidneys and urinary tract

Corticosteroids should be used with caution in patients with renal insufficiency.

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.

Effects on electrolytes and fluid balance

Systemic corticosteroids should be used with caution in patients with heart failure or hypertension. Medium and high doses of hydrocortisone or cortisone can lead to increased blood pressure, salt and water retention and increased potassium secretion. These effects are less likely with synthetic derivatives, except when used in high doses. Dietary restrictions with lower salt intake and potassium supplementation may be necessary.

All corticosteroids increase calcium excretion.

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.

Tumour lysis syndrome (TLS)

Tumour lysis syndrome (TLS) has been reported post-marketing in patients with malignancies, including haematological malignancies and solid tumours, following the use of systemic corticosteroids alone or in combination with other cytotoxic agents. Patients at high risk for TLS, such as patients with tumours that have a high rate of cell division, high tumour burden, and high sensitivity to cytotoxic agents, should be closely monitored and appropriate precautions taken.

Use in children

Corticosteroids cause growth retardation in infants, children and adolescence, therefore avoid long-term treatment with pharmacological doses. If long-term treatment is required, the infant / child's growth and development should be closely monitored (see section 4.2). Infants and children who are on long-term corticosteroid therapy are at particular risk of developing elevated intracranial pressure.

Excipients

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

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

The following combinations with Prednisolone may require dose adjustment.

Phenobarbital, phenytoin, carbamazepine:
Phenobarbital (which is also the metabolite of primidone), phenytoin and carbamazepine alone and in combination, induces the metabolism of hydrocortisone, prednisolone and methylprednisolone (shown in children with asthma) with increased dose requirements as a result. The interaction probably applies to the whole group of glucocorticoids.

Non-steroidal anti-inflammatory drugs:
1) The incidence of gastrointestinal bleeding and ulceration may increase if corticosteroids are given with NSAIDs.

2) Corticosteroids may increase the clearance of high doses of acetylsalicylic acid, which may lead to lower salicylate levels in the serum. Salicylate levels in serum may increase upon discontinuation of corticosteroid therapy, which could lead to an increased risk of toxic effects of salicylate.

Diabetes drugs:
Glucocorticoids increase blood sugar levels. Patients with diabetes mellitus receiving concomitant insulin and / or oral hypoglycaemic agents may need to adjust the dose of such treatment.

Oestrogens (also oral contraceptives containing oestrogens):
Oestrogens increase the concentration of transcortin. The effect of glucocorticoids that bind to transcortin can be enhanced and dose adjustments may be needed if oestrogens are added or removed from a stable treatment regimen.

Potassium Reducing Agents:
Potassium-reducing diuretics (e.g., thiazides, furosemide, ethacrynic acid) and other drugs that reduce the amount of potassium such as amphotericin B, xanthines and beta2-agonists, may potentiate the potassium-lowering effect of glucocorticoids. Serum potassium should be closely monitored in patients receiving glucocorticoids and potassium reducing agents.

Rifampicin:
Rifampicin induces the microsomal oxidation of glucocorticoids (hydrocortisone, prednisolone, methylprednisolone). This leads to an increased steroid need during rifampicin treatment and reduced steroid need after such treatment.

Isoniazid:
Prednisolone also has a potential effect which results in increased acetylation rate and clearance of isoniazid.

Oral anticoagulants:
There are reports of altered effects of anticoagulants given concurrently with prednisolone. Prothrombin time (INR) should be monitored during treatment.

CYP3A inhibitors, including medicinal products containing cobicistat:
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.

Anticholinergic, neuromuscular blockers:
Corticosteroids may affect the effect of anticholinergics.
1) Acute myopathy has been reported with concomitant use of high doses of corticosteroids and anticholinergics such as neuromuscular blockers (see section 4.4).
2) Antagonism with the neuromuscular blocking effect of pancuronium and vecuronium has been reported in patients taking glucocorticosteroids. This interaction can be expected with all competitive neuromuscular blockers.

Anticholinesterases:
Interaction between glucocorticoids and anticholinesterases such as ambenonium, neostigmine and pyridostigmine may lead to significant potency in myasthenia gravis.

If possible, treatment with anticholinesterase should be discontinued at least 24 hours before administration of glucocorticoid.

Methotrexate: There is a small amount of evidence that use of corticosteroids and methotrexate simultaneously may cause increased methotrexate toxicity and possibly death, although this combination of drugs has been used very successfully.

4.6 Pregnancy and lactation

Fertility
Animal studies have shown that corticosteroids impair fertility (see section 5.3).

Pregnancy
In animal studies, corticosteroids have been shown to give rise to various types of malformations (palate gap, skeletal malformations, see section 5.3).

The relevance in humans is unknown.

After long-term treatment, reduced placental and birth weight have been observed in humans and animals.

In addition, there is a risk of adrenal cortex failure in the newborn during long-term treatment. Therefore, during pregnancy, corticosteroids should be given after special consideration.

Breast-feeding
Prednisolone passes into breast milk, but the risk of affecting the baby seems unlikely with therapeutic doses.

4.7 Effects on ability to drive and use machines

The effect of corticosteroids on the ability to drive and use machines has not been systematically investigated.

Side effects such as dizziness, visual disturbances and fatigue are possible after treatment with corticosteroids. In such adverse reactions, patients should not drive or use machines.

4.8 Undesirable effects

Apart from substitution therapy, corticosteroid treatment always involves an overdose compared to the physiological state. Side effects mainly occur with long-term treatment, but also depend on dose size and individual sensitivity.

The following side effects have been observed and reported during treatment with Prednisolone at the following frequencies: 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).

Organ system	**Common**	**Uncommon**	**Rare**	**Not known**
Infections and infestations	Opportunistic infection Activation of infection (e.g., tuberculosis)			
Blood and lymphatic system				Leukocytosis (due to redistribution of intravascular granulocytes)
Immune system disorders				Drug hypersensitivity Anaphylactic reaction

				Anaphylactoid reaction
Endocrine disorders	Inhibition of the hypothalamic-pituitary-adrenal (HPA) axis, Cushing-like symptoms. Growth retardation (in children)			Steroid withdrawal syndrome (see section 4.4) Pheochromocytoma-related crisis (see section 4.4)
Metabolism and nutrition disorders	Hypokalaemia Sodium retention Increased gluconeogenesis Catabolic effects Osteoporosis			Metabolic acidosis Fluid retention Hypokalaemic alkalosis Dyslipidaemia Reduced glucose tolerance (diabetes mellitus may deteriorate and latent diabetes become manifest) Lipomatosis Increased appetite (which can lead to weight gain)
Psychiatric disorders		Activation of previous mental disorders (high dose)	Depression, mania in patients without previously known mental illness	Affective disorder (includes euphoria, affective lability, drug-related, suicidal condition) Psychotic disorder (includes delusions, hallucinations and schizophrenia) Mental illness Personality change Confusion state Anxiety Mood swings Abnormal behaviour Insomnia Irritability
Nervous system disorders			Benign intracranial hypertension	Epidural lipomatosis Seizure Amnesia Cognitive disorder

				Dizziness Headache
Eye disorders		Cataract Glaucoma Vision, blurred (see also section 4.4)		Central serous chorioretinopathy (see section 4.4) Exophthalmos
Cardiac disorders				Heart failure (in sensitive patients) Bradycardia**
Vascular disorders	Oedema hypertension			Thromboembolic events
Respiratory, thoracic and mediastinal disorders				Hiccup
Gastrointestinal disorders				Peptic wound (possibly with perforation and bleeding) Intestinal perforation pancreatitis Ulcerative esophagitis abdominal distention Abdominal pain Diarrhoea Dyspepsia Nausea
Skin and subcutaneous tissue disorders	Skin atrophy Impaired wound healing			Angioedema Hirsutism Petechiae Ecchymosis Erythema hyperhidrosis Stretch marks Itching Urticaria Acne
Musculoskeletal and connective tissue disorders	Muscular Atrophy		Aseptic bone necrosis Tendon	Muscle weakness Myalgia Myopathy

			rupture	Pathological fracture Neuropathic arthropathy Arthralgia
Renal and urinary disorders				Acute renal crisis (Scleroderma renal crisis) *
Reproductive system and breast disorders				Irregular menstruation
General disorders and administration site conditions				Fatigue Malaise
Investigations				Increased calcium levels in the urine Elevated alanine aminotransferase Elevated aspartate aminotransferase Increased blood alkaline phosphatase Elevated blood urea Suppression of skin test reactions[1]

1 Not MedDRA term.

* Acute renal crisis (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%)

** Following high doses.

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 Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Reports of acute toxicity and / or death following glucocorticoid overdose are rare.

Possibly, acute overdose may aggravate preexisting disease states such as ulcers, electrolyte disorders, infections and oedema.

Treatment: Not usually required. If proper gastric emptying, with charcoal. In case of overdose, there is no specific antidote, but the treatment is supportive and symptomatic.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glucocorticoid ATC code: H02AB06

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

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

The mechanism of action is not yet fully understood.

5.2 Pharmacokinetic properties

Absorption

Prednisolone is rapidly absorbed into the gastro-intestinal tract when given Orally. Maximum plasma concentrations is achieved after1 to 2 hours after oral administration. The plasma half-life of 2-3 hours. Its initial absorption, but not total bioavailability, is affected by food.

Distribution

Prednisolone is highly bound to plasma proteins and has high affinity for the transcortin.
The volume of distribution and clearance are reported to increase with transition from low to medium doses.

Metabolism

Prednisolone is metabolised primarily in the liver to a biologically inactive compound.
Prednisolone can be reversibly converted to prednisone by 11β-hydroxysteroid dehydrogenase.

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

Elimination

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

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

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize Starch
Pregelatinated Maize Starch
Sodium Starch Glycollate
Magnesium Stearate

6.2 Incompatibilities

None stated

6.3 Shelf life

36 months all pack sizes

6.4 Special precautions for storage

Store in a dry place below 25°C.
Keep container well closed.

6.5 Nature and contents of container

Polypropylene or high density polystyrene con tainers with polypropylene or polythene lids and/or polyurethane or polythene inserts.
Pack sizes: 100 & 500

6.6 Special precautions for disposal

No special instructions

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited

Boumpoulinas 11, 3rd Floor

NICOSIA

CYPRUS

P.C. 1060

CYPRUS

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