SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Prednisolone 5 mg Orodispersible Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5mg of Prednisolone.
Excipient(s) with known effect
None.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Orodispersible tablets.
White to off white, round, flat, bevelled edged tablets with central concave depression on both the surfaces, having peppermint odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prednisolone is indicated in the management of all conditions deemed likely to benefit from short or long term glucocorticoid therapy. These include:

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

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

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

Skin conditions
Life-threatening or incapacitating skin conditions such as pemphigus and exfoliative dermatitis.

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

Gastro-intestinal disease
During acute exacerbation in ulcerative colitis and regional ileitis (Crohn's Disease).

Respiratory disease
Sarcoidosis (especially with hypercalcaemia), fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculosis chemotherapy.

Haematological disorders
Various blood dyscrasias eg selected cases of haemolytic anaemia, thrombocytopenic purpura.

Miscellaneous
Nephrotic syndrome.

4.2 Posology and method of administration

Posology

In adults and the elderly:

The lowest effective dose should be used for the minimum period in order to minimise side effects.

Paediatric population:

Prednisolone should be used only when specifically indicated, in a minimum dosage and for the shortest possible time.

The initial dosage of Prednisolone Orodispersible Tablets may vary from 5mg to 60mg or more 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 section 4.4).

In patients who have received more than physiological dose for systemic corticosteroids (approximately 7.5mg prednisolone or equivalent) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about hypothalamic-pituitary-adrenal (HPA) suppression, the dose of corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 7.5mg of prednisolone is reached, dose reduction should be slower to allow the HPA-axis to recover.

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

- patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.
- when a short course has been prescribed within one year of cessation of long-term therapy (months or years).
- patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy.
- patients receiving doses of systemic corticosteroid greater than 40mg daily of prednisolone (or equivalent).
- patients repeatedly taking doses in the evening. (See section 4.4 and 4.8).

During prolonged therapy, dosage may need to be temporarily increased during periods of stress or during exacerbations of the disease (see section 4.4) If there is lack of a satisfactory clinical response to Prednisolone Orodispersible Tablets, the drug should be gradually discontinued and the patient transferred to alternative therapy.

Intermittent dosage regimen: A single dose of Prednisolone Orodispersible Tablets in the morning on alternate days or at longer intervals is acceptable therapy for some patients. When this regimen is practical, the degree of pituitary-adrenal suppression can be minimised.

Specific dosage guidelines: The following recommendations for some corticosteroid-responsive disorders are for guidance only. Acute or severe disease may require initial high dose therapy with reduction to the lowest effective maintenance dose as soon as possible. Dosage reductions should not exceed 5-7.5mg daily during chronic

treatment.

Allergic and skin disorders: Initial doses of 5-15mg daily are commonly adequate.

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

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

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

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 section 4.4).

Paediatric population

Although appropriate fractions of the actual dose may be used, dosage will usually be determined by clinical response as in adults (see section 4.4). Alternate day dosage is preferable where possible.

Method of administration

For oral use. The tablet should be placed on the tongue, where it will dissolve and be swallowed with the saliva. The tablet should not be chewed and should not be swallowed undissolved.

The daily dose should be taken in the morning after breakfast. For further information reference to dosage see section 4.4 Special warnings and precautions for use.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1. Systemic infections unless specific anti-infective therapy is employed. Patients with ocular herpes simplex due to the possibility of perforation.

4.4 Special warnings and precautions for use

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

Patients/and or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 pharmacokinetic interactions that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary.

Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

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

- Diabetes mellitus or in those with a family history of diabetes.
- Glaucoma or in those with a family history of glaucoma.
- Hypertension or congestive heart failure.
- Liver failure.
- Epilepsy.
- Osteoporosis: This is of special importance in post-menopausal females who are at particular risk.
- Patients with a history of severe affective disorders and particularly those with a previous history of corticosteroid induced psychoses.
- Peptic ulceration.
- Previous steroid myopathy.
- Glucocorticoids should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy.
- Because cortisone has been reported rarely to increase blood coagulability and to precipitate intravascular thrombosis, thromboembolism, and thrombophlebitis, corticosteroids should be used with caution in patients with thromboembolic disorders.
- Renal insufficiency.

- Tuberculosis: Those with a history of, or X-ray changes characteristic of tuberculosis. The emergence of active tuberculosis can, however, be prevented by the prophylactic use of antituberculous therapy.
- Recent myocardial infarction (rupture).
- Chickenpox: Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunisation with varicella/zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants special care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased.
- Measles: Patients are advised to avoid exposure to measles, medical advice should be sought if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.
- Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.
- The effect of corticosteroids may be enhanced in patients with hypothyroidism in those with chronic liver disease with impaired hepatic function.
- Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.
- Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Scleroderma renal crisis

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

Withdrawal

In patients who have received more than physiological doses of systemic corticosteroids (approximately 7.5mg prednisolone or equivalent) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 7.5mg of prednisolone is reached, dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt withdrawal of doses of up to 40mg daily of prednisolone, or equivalent for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients.

In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

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

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

Use in 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.

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.

This product should not be taken with grapefruit or grapefruit juice (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

Hepatic microsomal enzyme inducers: Drugs that induce hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4 such as phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminoglutethimide may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism. Lack of expected response may be observed and dosage of Prednisolone Orodispersible Tablets may need to be increased.

Hepatic microsomal enzyme inhibitors: Drugs that inhibit hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4 (e.g. ketoconazole, troleandomycin) may decrease glucocorticoid clearance. Dosages of glucocorticoids given in combination with such drugs may need to be decreased to avoid potential adverse effects.

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

Non-steroidal anti-inflammatory drugs: Concomitant administration of ulcerogenic drugs such as indomethacin during corticosteroid therapy may increase the risk of GI ulceration. Aspirin should be used cautiously in conjunction with glucocorticoids in patients with hypoprothrombinaemia. Although concomitant therapy with salicylate and corticosteroids does not appear to increase the incidence or severity of GI ulceration, the possibility of this effect should be considered. Serum salicylate concentrations may decrease when corticosteroids are administered concomitantly. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Salicylates and corticosteroids should be used concurrently with caution. Patients receiving both drugs should be observed closely for adverse effects of either drug.

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

Anticoagulants: Response to anticoagulants may be reduced or less often, enhanced by corticosteroids. Close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Antiepileptics: Carbamazepine, phenobarbital, phenytoin and primidone accelerate metabolism of corticosteroids and may reduce their effect.

Antifungals: Risk of hypokalaemia may be increased with amphotericin, therefore concomitant use with corticosteroids should be avoided unless corticosteroids are required to control reactions; ketoconazole inhibits metabolism of methylprednisolone and possibly other corticosteroids.

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

Cardiac Glycosides: Increased toxicity if hypokalaemia occurs with corticosteroids.

Ciclosporin: Concomitant administration of prednisolone and ciclosporin may result in decreased plasma clearance of prednisolone (i.e. increased plasma concentration of prednisolone). The need for appropriate dosage adjustment should be considered when these drugs are administered concomitantly.

Cytotoxics: Increased risk of haematological toxicity with methotrexate.

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

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

Oestrogens: Oestrogens may potentiate the effects of glucocorticoids and dosage adjustments may be required if oestrogens are added to or withdrawn from a stable dosage regimen.

Somatropin: Growth promoting effect may be inhibited.

Sympathomimetics: Increased risk of hypokalaemia if high doses of corticosteroids given with high doses of bambuterol, fenoteral, formoteral, ritodrine, salbutamol, salmeterol and terbutaline.

Grapefruit or grapefruit juice

The consumption of grapefruit and grapefruit juice, known inhibitors of CYP3A4, should be avoided while taking prednisolone due to the risk of grapefruit-induced increase in plasma prednisolone concentrations and adverse effects related to this (see section 4.4).

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

4.6 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. 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 nongravid state.

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

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 receiving 40mg or more daily should be monitored for signs of adrenal suppression but the benefits of breast feeding are likely to outweigh any theoretical risk.

Fertility

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

4.7 Effects on ability to drive and use machines

There is no evidence to suggest that prednisolone has any effect on the ability to drive or use machines.

4.8 Undesirable effects

A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood, and suicidal thoughts), psychotic reactions

(including mania, delusions, hallucinations, and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is Not known.

The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment (see section 4.4).

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	**Frequency**	**Undesirable effects**
Infections and infestations	Not known	Increases susceptibility to and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see section 4.4).
Blood and lymphatic system	Not known	Leukocytosis
Immune system disorders	Not known	Hypersensitivity including anaphylaxis
Endocrine disorders	Not known	Cushingoid, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of latent diabetes mellitus
Metabolism and nutrition disorders	Not known	Sodium and water retention, increased appetite which may result in weight gain, alkalosis hypokalaemic, negative nitrogen and calcium balance.
Psychiatric disorders	Not known	Euphoric mood, drug dependence, depression, insomnia, schizophrenia
Nervous system disorders	Not known	Dizziness, headache, epilepsy
Eye disorders	Not known	Glaucoma, papilloedema, cataract subcapsular, central serous chorioretinopathy, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease and vision, blurred (see also section 4.4)
Ear and labyrinth disorders	Not known	Vertigo

Cardiac disorders	Not known	Congestive heart failure in susceptible patients, bradycardia***
Vascular disorders	Not known	Thromboembolism, hypertension
Gastrointestinal disorders	Not known	Dyspepsia, nausea, peptic ulcer with perforation and haemorrhage, abdominal distension, abdominal pain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, pancreatitis acute
Skin and subcutaneous tissue disorders	Not known	Hirsutism, skin atrophy, bruising, skin striae, telangiectasia, acne, hyperhidrosis, may suppress reactions to skin tests, pruritis, rash, urticaria
Musculoskeletal and connective tissue disorders	Not known	Myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, myalgia
Renal and urinary disorders	Not known	Scleroderma renal crisis*
Reproductive system and breast disorders	Not known	Menstrual irregularity and amenorrhoea
General disorders and administration site conditions	Not known	Impaired healing, withdrawal symptoms**, fatigue, malaise
Investigations	Not known	Weight increased, increased intra-ocular pressure
Injury, poisoning and procedural complications	Not known	Tendon rupture

*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%)

***Withdrawal symptoms:** Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4 and 4.2). A steroid “withdrawal syndrome” seemingly unrelated to adrenocortical insufficiency may also occur following abrupt discontinuance of glucocorticoids.

This syndrome includes symptoms such as: anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules weight loss, and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels.

***Following high doses

Additional side effects in children and adolescents

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.

Raised intracranial pressure with papilloedema (pseudotumor cerebri) in children, usually after treatment withdrawal.

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

Symptoms

Reports of acute toxicity and/or death following overdosage of glucocorticoids are rare.

Management

No specific antidote is available, treatment is supportive and symptomatic.

Serum electrolytes should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteriods for systematic use, plain

ATC code: H02AB06

Mechanism of action

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogues 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 responses to diverse stimuli.

5.2 Pharmacokinetic properties

Absorption

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

Distribution

Prednisolone shows dose dependent 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.

Biotransformation

Prednisolone is mainly metabolised 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.

Elimination

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

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

Dextrates (hydrated)
Colloidal hydrated silica
Basic butylated methacrylate copolymer (Eudragit E 100)
Hypromellose (3 cps)
Isopropyl alcohol
Purified water
Purified talc
Mannitol 200
Croscarmellose sodium
Cellulose microcrystalline
Sucralose
Magnesium stearate
Peppermint flavour (containing maize maltodextrin, natural flavouring complexes and E 1450 Modified corn starch)

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25°C.

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Alu-Alu blisters packed into cartons of 30 or 100 tablets.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Kent Pharma UK Limited
2nd Floor
Connect 38
1 Dover Place
Ashford
Kent

England
TN23 1FB

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