PREDNELAN™

Prednisolone

QUALITATIVE AND QUANTITATIVE COMPOSITION

Prednelan™ 5mg tablet: Each tablet contains prednisolone BP 5 mg
Prednelan™ 20mg tablet: Each tablet contains prednisolone BP 20 mg

CLINICAL PARTICULARS

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 dyscrasiaseg selected cases of haemolyticanaemia, thrombocytopenic purpura.

Miscellaneous: Nephrotic syndrome.

Posology and method of administration

Adults

20-40mg daily (acute conditions up to 80mg daily) reducing gradually to maintenance level when symptoms have subsided. Maintenance dosage is usually 5-20mg daily reached in about two weeks by reduction of the daily dosage by 5mg or 2.5mg, two or three times a week.

Children

Fractions of adult dosage may be used (eg 75% at 12 years, 50% at 7 years and 25% at 1 year), but clinical factors must be taken into consideration.

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

Elderly

Treatment of elderly patients, especially if long-term, should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age, particularly diabetes, hypertension, hypokalaemia, osteoporosis, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

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

For oral administration

Contraindications

Hypersensitivity to any ingredients in the formulation.

Systemic infections unless specific anti-infective therapy is employed.

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

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.

Visual disturbance: Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient present 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.

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.
- 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. Propylaxis 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.

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.

Interaction with other medicinal products and other forms of interaction

•Antacids can reduce the absorbtion of prednisolone if given in high doses.Indigestion remedies should not be taken at the same time of day as Prednisolone.

•Rifampicin, rifabutin, carbamazepine, phenobarbital, phenytoin, primidone, carbimazole and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced. Therefore it may be necessary to adjust the dose of prednisolone accordingly.

•The desired effects of hypoglycaemic agents (including insulin), antihypertensives and diuretics are antagonised by corticosteroids.

•The hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, beta-2-agonists, theophylline and carbenoxolone are enhanced.

•The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

•Ciclosporin increases the plasma concentration of prednisolone.

•The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

•NSAIDs such as indometacin may increase the risk of GI ulceration. The possiblity of GI ulceration should be considered with concomitant use with any other NSAIDs.

•Aspirin should be used cautiously in conjunction with glucocorticoids in patients with hypoprothrombinaemia. Concurrent use of aspirin and prednisolone may result in an increased risk of gastrointestinal ulceration and subtherapeutic aspirin serum concentrations.

•Antifungals: Increased risk of hypokalaemia with amphotericin. Avoid concomitant use. Ketoconazole reduces the metabolic and renal clearances of methylprednisolone, this may also occur with prednisolone.

•Mifepristone reduces the effect of corticosteroids for 3-4 days after administration.

•Methotrexate may have a steroid sparing effect. There is evidence that the toxicity of methotrexate is increased.

•Etoposide metabolism may be inhibited by corticosteroids in vitro. This may lead to an increase in both efficacy and toxicity of the etoposide. Monitoring would be prudent.

•Corticosteroids should not be used concurrently with retinoids and tetracyclines due to increased intracranial pressure.

•Oestrogens and progestogens increase plasma concentrations of corticosteroids.

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 intrauterine growth retardation. Hypoadrenalism may occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. Cataracts have also been rarely reported. 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 abnormal pregnancies may be treated as though they were in the non-gravid state.

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

Lactation

Corticosteroids are excreted in small amounts in breast milk. 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 out-weigh any theoretical risk. Monitoring of the infant for adrenal suppression is advised.

Effects on ability to drive and use machines

If insufficient sleep occurs, the likelihood of impaired alertness may be increased, patients should make sure they are not affected before driving or operating machinery.

Undesirable effects

The incidence of predictable undesirable effects, including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and the duration of treatment (see “other special warnings and precautions”). Undesirable effects may be minimised by using the lowest effective dose for the minimum period, and by administering the daily requirement as a single morning dose or whenever possible as a single morning dose on alternative days. Frequent patient review is required to appropriately titrate the dose against disease activity.

Anti-inflammatory/immunosuppressive: Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis. See “other special warnings and precautions”.

Gastrointestinal: Abdominal distension, acute pancreatitis, dyspepsia, nausea, increased appetite, oesophageal candidiasis, oesophageal ulceration, peptic ulceration with perforation and haemorrhage, perforation of the small bowel, particularly in patients with inflammatory bowel disease.

Endocrine/metabolic: Cushingoid facies, growth suppression in infancy, childhood and adolescence, hirsutism, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, menstrual irregularity and amenorrhoea, negative protein and calcium balance, suppression of the hypothalamo-pituitary adrenal axis, and weight gain. Although the frequency is not known, there is a risk for Cushing Syndrome.

Fluid and electrolyte disturbance: Hypertension, nocturia, hypokalaemic alkalosis, potassium loss, sodium and water retention, risk of congestive heart failure in susceptible patients.

Musculoskeletal: Avascular osteonecrosis, osteoporosis, proximal myopathy, tendon rupture, vertebral and long bone fractures, muscle weakness, wasting and loss of muscle mass.

Dermatological: Acne, bruising, impaired healing, skin atrophy, striae, telangiectasia.

Neuropsychiatric: 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), marked euphoria leading to dependence; aggravation of epilepsy, behavioural disturbances, irritability, nervousness, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be 5-6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

Intracranial pressure with papilloedema in children (pseudotumourcerebri) usually after treatment withdrawal, psychological dependence.

Ophthalmic: Corneal or scleral thinning, scleral perforation, exacerbation of ophthalmic viral or fungal disease, glaucoma, increased intra-ocular pressure, papilloedema, posterior subcapsular cataracts, central serous chorioretinopathy (frequency not know known).

General: Hypersensitivity including anaphylaxis, leucocytosis, malaise, thromboembolism.

Withdrawal symptoms: Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. See “other special warnings and precautions”. A “withdrawal syndrome” may also occur including arthralgia, conjunctivitis, fever, loss of weight, myalgia, painful itchy skin nodules and rhinitis.

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

Overdose

In the event of an overdosage, supportive and symptomatic therapy is indicated.

Serum electrolytes should be monitored.

Pharmacological properties

Pharmacodynamic properties

ATC CODE: H02A B06

Prednisolone is one of the highly potent glucocorticoid steroids having anti-inflammatory, hormonal and metabolic effects qualitatively similar to those of hydrocortisone.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

Pharmacokinetic properties

Absorption: Prednisolone is readily and almost completely absorbed from the GI tract after oral administration.

Distribution: Peak plasma concentrations are obtained 1-2 hours after oral administration. Prednisolone is extensively bound to plasma proteins, although less so than hydrocortisone. Prednisolone crosses the placenta and small amounts are excreted in breast milk.

Metabolism: Prednisolone is mainly metabolised in the liver and has a usual plasma half-life of 2-3 hours. It has a biological half-life lasting several hours which makes it suitable for the alternate-day administration regimens which have been found to reduce the risk of adrenocortical insufficiency, yet provide adequate corticosteroid coverage in some disorders.

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

Excretion: It is excreted in the urine as free and conjugated metabolites, together with an appreciable proportion of unchanged prednisolone.

Preclinical safety data

Not applicable.

Pharmaceutical particulars

List of excipients

Lactose, Maize Starch, Gelatin, Magnesium Stearate.

Incompatibilities

None known.

SHELF LIFE

Prednelan Tablets 5mg 500's: 30 months

Prednelan Tablets 20mg 100's: 24 months

SPECIAL PRECAUTIONS FOR STORAGE

Prednisolone Tablets should be stored in a dry place below 30°C and protected from light.

Keep all medicine out of reach of children.

NATURE AND CONTENTS OF CONTAINER

Prednelan Tablets 5mg: 50x10's in alu-alu strips

Prednelan Tablets 20mg: 10 x 10's in alu-alu strips

MANUFACTURED BY:

GlaxoSmithKline Bangladesh Limited

Fouzderhat Industrial Area, Chittagong

Ref

https://www.medicines.org.uk/emc/medicine/24130

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