

# DATA SHEET

## PREDNISONONE

1 mg, 2.5 mg, 5 mg and 20 mg tablets

### Presentation

**Prednisone 1 mg tablet:** White, or almost white, round tablet with one face embossed "1" and the other embossed "P". Diameter 6.25mm.

**Prednisone 2.5 mg tablet:** White, or almost white, round tablet with one face embossed "2.5" and the other embossed "P". Diameter 6.25mm.

**Prednisone 5 mg tablet:** White, or almost white, round tablet with one face embossed "5" and the other embossed "P". Diameter 6.25mm.

**Prednisone 20 mg tablet:** Pink, round tablet with a bisecting score on one face and a "P" on the other. Diameter 6.25mm. Prednisone 20mg tablets contain FD & C Red No.3 colouring.

Prednisone tablets are gluten-free.

### Uses

#### *Actions*

Prednisone is a synthetic glucocorticoid obtained by dehydrogenation of cortisone at positions 1 and 2. It is biologically inert.

Anti-inflammatory, immunosuppressant and mineralcorticoid properties are only exhibited when prednisone is converted to prednisolone in the liver.

Prednisolone is extensively bound to plasma proteins although less so than hydrocortisone (cortisol). Prednisolone is a potent therapeutic agent influencing the biochemical behaviour of most tissues of the body. Unlike hydrocortisone, prednisolone has little sodium retaining activity.

Prednisolone has a biological half-life lasting several hours, intermediate between those of cortisone (cortisol) and the longer acting glucocorticoids, such as dexamethasone. It is this intermediate duration of action 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.

## ***Pharmacokinetics***

Prednisone is readily absorbed from the gastrointestinal tract and is then converted to its active metabolite prednisolone, by hydrogenation of the ketone group at position 11, in the liver. The preconversion biological half-life of prednisone is about 60 minutes.

Prednisolone is excreted in the urine as free and conjugated metabolites together with an appreciable proportion of unchanged prednisolone. Prednisolone has a usual plasma half-life of 2 to 4 hours.

A recent review of the pharmacokinetics of prednisone and prednisolone concluded that the conversion of prednisone is probably not diminished by liver disease.

## ***Indications***

Prednisone is indicated wherever corticosteroid therapy is considered necessary eg.

**Skin:** Pemphigus vulgaris, allergic dermatitis, eczema, exfoliative dermatitis, dermatitis herpetiformis, dermatitis medicamentosa, erythema multiforme, disseminated lupus erythematosus, dermatomyositis, polyarteritis nodosa.

**Respiratory:** Severe bronchial asthma and status asthmaticus, emphysema, pulmonary fibrosis.

**Adrenal:** Adrenal hyperplasia (adrenogenital syndrome).

**Haematological:** Idiopathic thrombocytopenic purpura, acquired haemolytic anaemia, acute leukaemia.

**Other:** Nephrotic syndrome, iridochoroiditis ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, rheumatic fever, gout, peri-arthritis of the shoulder.

## **Dosage and Administration**

Prednisone is intended for oral administration only.

**Adults:** The initial dose is 5mg to 80mg daily depending on the condition being treated, as a single dose after breakfast, as divided doses, or as a double dose on alternate days. The maintenance dose is usually 5mg to 20mg daily. The dose should be individualised according to the severity of the disease and the patients response rather than by age or body weight.

For adrenogenital syndrome: 5 to 10mg a day as a single dose.

The usual adult prescribing limit is up to 250mg day.

**Children:** For children up to 18 months of age, dosage has not been established. For children over 18 months, initial dosage is 0.5mg/kg daily, this dosage can be doubled or trebled if necessary, continued until definitive remission occurs. Maintenance dose 0.125 to 0.25mg/kg daily.

A single daily dose is preferable over divided doses, to reduce the likelihood of adrenal suppression. The dose should be taken prior to 9am, to closely mimic the body's own maximum corticosteroid secretion. Giving the dose, usually double pre-determined daily dose, on alternate mornings may also reduce the suppression of the HPA axis. This regimen is not recommended for treatment of haematologic disorders, malignancies, ulcerative colitis, or severe conditions.

Patients with known or suspected renal insufficiency, including those already receiving replacement therapy require an increase in dosage or reinstatement of therapy prior to, during and for a time following exposure to stress.

## **Contraindications**

Prednisone is contraindicated in patients with: peptic ulcer, osteoporosis, psychoses or severe psychoneuroses. Prednisone is usually contraindicated in the presence of acute infection, unless the patient is on long term prednisone whereupon the dose should be increased to counteract the increased stress of the infection.

Administration of live virus vaccines including smallpox is contraindicated in patients receiving immunosuppressive doses of prednisone since the expected serum antibody response may not be obtained.

Immunisation procedures may, however, be undertaken in patients who are receiving corticosteroids as replacement therapy.

Known hypersensitivity to prednisone, or any of the excipients in the tablet.

## **Warnings and Precautions**

### General Precautions

Caution is necessary when oral corticosteroids are used in patients with the following conditions and frequent monitoring is necessary:

- Hypertension
- Hypothyroidism
- Congestive Heart failure or recent myocardial infarction
- Liver failure
- Renal insufficiency
- Diabetes mellitus or in those with a family history of diabetes
- Osteoporosis
- Glaucoma
- Patients with a history of severe affective disorders particularly of steroid induced psychoses

- Epilepsy and/or seizure disorder
- Peptic ulceration
- Previous steroid myopathy
- Tuberculosis
- Patients with myasthenia gravis receiving anticholinesterase therapy since prednisone may decrease plasma anticholinesterase activity
- Patients with thromboembolic disorders
- Patients with Duchenne's muscular dystrophy since transient rhabdomyolysis and myoglobinuria have been reported following strenuous physical activity
- Patients with Cushing's disease

### Adrenocortical Insufficiency

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration and duration of therapy.

Symptoms of adrenal insufficiency include: malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration.

During prolonged courses of corticosteroid therapy sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of fluid intake and output and daily weight records may give an early warning of fluid retention.

Acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly, therefore withdrawal of prednisone should always be gradual. A degree of adrenal insufficiency may persist for 6 to 12 months; therefore in any situation of stress occurring during that period steroid therapy may need to be reinstated. Since mineralocorticoid secretion may be impaired treatment with salt and/or a mineralocorticoid may also be needed.

During prolonged therapy, any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage.

### Anti-inflammatory/ Immunosuppressive effects and Infection

Suppression of the inflammatory response and immune function increases 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 recognized when corticosteroids including prednisone are used. The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

Chickenpox is of particular concern since this 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 urgent medical attention. Passive immunization is recommended for non-

immune patients who do come into contact with chickenpox. If a diagnosis of chickenpox is confirmed the illness warrants specialist care and urgent treatment.

Live vaccines are contraindicated in individuals on high doses of corticosteroids and should be postponed until at least 3 months after stopping corticosteroid therapy.

### Ocular Effects

Prolonged use of corticosteroids may produce subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves.

Corticosteroids should only be initiated in patients with ocular herpes simplex with appropriate viral cover by ophthalmologists because of the risk of corneal scarring loss of vision and corneal perforation.

### Psychiatric effects

Patients and/or carers should be warned that potentially severe psychiatric reactions may occur. Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients and/or 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 prednisone in patients with existing or previous history of severe affective disorders.

Psychic derangements range from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations.

### Use in Children

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.

Children and adolescents should also be closely monitored for osteoporosis, avascular necrosis of the femoral heads, glaucoma or cataracts during prolonged therapy.

Children are at special risk from raised intracranial pressure.

### Use in the elderly

Long-term use in the elderly should be planned bearing in mind the more serious consequences of the common side-effects of prednisone in old age, especially osteoporosis, diabetes, hypertension, hypokalaemia, susceptibility to infection and thinning of the skin. Close medical supervision is required to avoid life threatening reactions.

Geriatric patients especially post menopausal women may be more likely to develop glucocorticoid induced osteoporosis.

#### Other

The withdrawal symptoms may simulate a clinical relapse of the disease for which the patient is undergoing treatment. Withdrawal of prednisone should always be gradual, the rate depending upon the individual patients response, the dose and duration of therapy.

Corticosteroid induced elevation of blood pressure, salt and water retention and increased potassium excretion are possible with high doses of prednisone. Like all corticosteroids, prednisone increases calcium excretion.

It has been observed that in cerebral malaria, the use of corticosteroids was associated with prolongation of coma and a higher incidence of pneumonia and gastro-intestinal bleeding. Corticosteroids may activate latent amoebiasis, therefore, it is recommended that latent or active amoebiasis be ruled out before initiating corticosteroid treatment in any patient who has spent time in the tropics or has unexplained diarrhoea.

The use of prednisone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis. The prednisone must be used in conjunction with an appropriate antituberculosis regimen.

Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients.

The use of corticosteroids may cause psychic derangements ranging from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations.

Corticosteroids should be used with caution in non-specific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection.

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Patients who have received high or prolonged doses of prednisone should be given supplementary corticosteroids to overcome periods of stress caused by anaesthesia, surgery or trauma.

**Use in Pregnancy and Lactation:** Since adequate information on the effects of prednisone on the developing child is not known, use in pregnancy or in women of child-bearing potential requires that the possible benefit of cortisone to the mother be weighed against the potential hazards to the mother and/or foetus.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production or cause other unwanted effects. Mothers should, therefore, be advised not to nurse if corticosteroids are required.

**Embryotoxicity, teratogenicity, carcinogenicity, mutagenicity:** Teratogenic effects of glucocorticoids which have been demonstrated in animal studies since 1950 have not been confirmed in man. Use of glucocorticoids in man has not shown an increase in malignant disease.

## **Adverse Effects**

*Body as a whole:* leucocytosis, hypersensitivity including anaphylaxis, thromboembolism, fatigue, malaise

*Cardiovascular:* congestive heart failure in susceptible patients, hypertension

*Gastro-intestinal:* dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis

*Musculoskeletal:* proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, myalgia

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

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

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

*Nervous system:* euphoria, psychological dependence, depression, insomnia, dizziness, headache, vertigo, raised intracranial pressure with papilloedema in children, usually after treatment withdrawal. Aggravation of schizophrenia, Aggravation of epilepsy suicidal ideation, mania, delusions, hallucinations, irritability anxiety, insomnia and cognitive dysfunction. In adults the frequency of severe psychiatric reactions has been estimated to be 5-6%.

*Eye disorders:* increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease

*Anti-inflammatory and Immunosuppressive effects:* increased susceptibility to and severity of infections with suppression of clinical symptoms and signs. Opportunistic infections, recurrence of dormant tuberculosis.

*Withdrawal symptoms :* too rapid a reduction of prednisone following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A steroid

withdrawal syndrome seemingly unrelated to adrenocortical insufficiency may also occur and include symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, weight loss, and/or hypotension.

## **Interactions**

### Hepatic microsomal enzyme inducers

Medicines that induce hepatic enzyme cytochrome P-450 isozyme 3A4 such as Phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminogluethimide may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism.

### Hepatic microsomal enzyme inhibitors

Medicines that inhibit hepatic enzyme cytochrome P-450 isozyme 3A4 such as ketoconazole, ciclosporin or ritonavir may decrease glucocorticoid clearance. A reduction in prednisone dose may be needed to reduce the risk of adverse effects.

### Antidiabetic Agents

Prednisone may increase blood glucose levels. Patients may need dosage adjustment of any concurrent antidiabetic therapy.

### Non-steroidal anti-inflammatory drugs (NSAIDs)

Concomitant administration may increase the risk of GI ulceration. Aspirin should be used cautiously in conjunction with prednisone in patients with hyp thrombinaemia. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Patients should be observed closely for adverse effects of either medicine.

### Anticoagulants

Response to anticoagulants may be reduced or less often enhanced by corticosteroids. Close monitoring of the INR or prothrombin time is recommended.

### Antifungals

The risk of hypokalaemia may be increased with amphotericin.

### Cardiac glycosides

There is a risk of toxicity if hypokalaemia occurs due to prednisone treatment.

### Cytotoxic agents

There is an increased risk of haematological toxicity when prednisone is given with methotrexate.

### Mifepristone

The 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. The dose of prednisone may need to be adjusted if oestrogen therapy is commenced or stopped.

#### Somatropin

The growth promoting effect may be inhibited.

#### Sympathomimetics

There is an increased risk of hypokalaemia if high doses of corticosteroids are given with high doses of salbutamol, salmeterol, terbutaline or formoterol.

#### Diuretics

*Excessive potassium loss may be experienced if glucocorticoids and potassium-depleting diuretics (such as frusemide and thiazides) or carbonic anhydrase inhibitors (such as acetazolamide) are given together.*

#### Antacids

*Concurrent use of antacids with prednisone may decrease absorption of these glucocorticoids – efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of prednisone.*

### **Overdosage**

Adverse effects related to prednisone normally develop only after prolonged use of doses in excess of the normal physiological requirement. Treatment is symptomatic and where possible the prednisone dose should be reduced gradually.

### **Pharmaceutical Precautions**

Store at or below 30 °C. Protect from light and moisture and keep out of reach of children.

### **Medicine Classification**

Prescription Medicine.

### **Package Quantities**

Prednisone 1 mg and 2.5 mg tablets are in packs of 100. Prednisone 5 mg tablets in packs of 30, 100 and 500. Prednisone 20 mg tablets are in packs of 30 and 100.

### **Further Information**

Prednisone is 17,21-dihydroxypregna-1,4-diene 3,11,20 trione. It has a molecular weight of 358.4 and its molecular formula is C<sub>21</sub>H<sub>26</sub>O<sub>5</sub>.

Other ingredients of the tablets are: Lactose, Maize cornflour, Polyvinylpyrrolidinone, Magnesium stearate, Talc and Sodium starch glycolate. Prednisone 20mg tablets contain FD & C Red No.3 colouring.

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### **Date of Preparation**

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