

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

DELTACORTRIL ENTERIC 5 mg gastro-resistant tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg of prednisolone.

Also contains 31.6mg of lactose

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Gastro-Resistant Tablet

Smooth, uniformly coloured maroon tablets

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

**Allergy and anaphylaxis:** Bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema, anaphylaxis.

**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 and secondary adrenal insufficiency, congenital adrenal hyperplasia.

**Gastro-intestinal disorders:** 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.

**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.

**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.

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

**Skin disorders:** Pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, pyoderma gangrenosum.

**Miscellaneous:** Sarcoidosis, hyperpyrexia, Behçets disease, immunosuppression in organ transplantation.

#### 4.2 Posology and method of administration

The initial dosage of Deltacortril Enteric may vary from 5mg to 60mg daily 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 'Special warnings and special precautions for use').

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 'Special Warnings and Special Precautions for use' and 'Undesirable effects')

During prolonged therapy, dosage may need to be temporarily increased during periods of stress or during exacerbations of the disease (See 'Special Warnings and Special Precautions for Use').

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

**Intermittent dosage regimen:** A single dose of Deltacortril Enteric 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 children:** Although appropriate fractions of the actual dose may be used, dosage will usually be determined by clinical response as in adults (see also "Special Warnings and Special Precautions for Use"). Alternate day dosage is preferable where possible.

**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 "Special Warnings and Special Precautions for Use").

#### 4.3 Contraindications

Systemic infections unless specific anti-infective therapy is employed. Hypersensitivity to any ingredient. Ocular herpes simplex because of possible perforation.

#### 4.4 Special warnings and precautions for use

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

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 oral corticosteroids, including Deltacortril Enteric, are prescribed in patients with the following conditions, and frequent patient monitoring is necessary.

- Tuberculosis: Those with a previous history of, or X-ray changes characteristic of, tuberculosis. The emergence of active tuberculosis can, however, be prevented by the prophylactic use of anti-tuberculosis therapy.
- Hypertension.
- Congestive heart failure.
- Liver failure.
- Renal insufficiency.
- Diabetes mellitus or in those with a family history of diabetes.
- 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 steroid-induced psychoses.
- Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids including prednisolone
- Epilepsy and/or seizure disorders
- 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.

**A Patient Information Leaflet is supplied with this product.**

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 on alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity. (See 'Posology and method of administration').

**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 glucocorticoid therapy.

In addition, acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly. Drug-induced secondary adrenocortical insufficiency may therefore be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstated.

Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently. 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 re-introduced.

Patients should carry Steroid treatment cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.

**Anti-inflammatory/Immunosuppressive effects and Infection:** 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 infection such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised when corticosteroids including prednisolone are used. The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

**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 specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased. The effect of corticosteroids may be enhanced in patients with hypothyroidism and in those with chronic liver disease with impaired hepatic function.

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

**Administration of Live Vaccines:** Live vaccines should not be given to individuals on high doses of corticosteroids, due to impaired immune response. Live vaccines should be postponed until at least 3 months after stopping corticosteroid therapy. (See also section 4.5 Interactions.)

**Ocular Effects:** Prolonged use of corticosteroids may produce posterior 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.

Establishment of secondary fungal and viral infections of the eye may also be enhanced in patients receiving glucocorticoids. Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible perforation.

**Cushing's disease:** Because glucocorticoids can produce or aggravate *Cushing's syndrome*, glucocorticoids should be avoided in patients with Cushing's disease.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis. Psychic derangements may appear when corticosteroids, including prednisolone, are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations.

**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.

**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.

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

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

#### 4.5 Interaction with other medicinal products and other forms of interactions

**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 Deltacortril Enteric 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.

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.

**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.

**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.

**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.

**Somatropin:**Growth promoting effect may be inhibited.

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

**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.

**Other:**The desired effects of 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**

**Use in 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. Cataracts have been observed in infants born to mothers treated with long-term prednisolone during pregnancy. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

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

**Use in lactation:** Corticosteroids are excreted in small amounts in breast milk. Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants.

Since adequate reproductive studies have not been performed in humans with glucocorticoids, these drugs should be administered to nursing mothers only if the benefits of therapy are judged to outweigh the potential risks to the infant.

#### 4.7 Effects on ability to drive and use machines

The effect of Deltacortril Enteric on the ability to drive or use machinery has not been evaluated. There is no evidence to suggest that prednisolone may affect these abilities.

#### 4.8 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 'Special warnings and special precautions for use').

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 unknown.

Undesirable effects listed in the table are grouped by MedDRA System Organ Classes.

Undesirable effects are ranked under heading of frequency, using the following convention, when applicable: very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $<1/10$ ); uncommon ( $\geq 1/1,000$  to  $<1/100$ ); rare ( $\geq 1/10,000$  to  $<1/1000$ ); very rare ( $<1/10,000$ ); not known (cannot be estimated from the available data).

System Organ class	Adverse reaction	Frequency
Cardiac disorders	Congestive heart failure in susceptible patients. Bradycardia* *Following high doses	Not known
Gastrointestinal disorders	Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis.	Not known
Musculoskeletal and connective tissue disorders	Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, myalgia, growth suppression in infancy, childhood and adolescence	Not known
Metabolism and nutrition disorders	Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen and calcium balance, increased appetite which may result in weight gain	Not known
Skin and subcutaneous tissue disorder	Hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, may suppress reactions to skin tests, pruritis, rash, urticaria	Not known

Endocrine disorders	Suppression of the hypothalamo-pituitary adrenal axis particularly in times of stress, as in trauma, surgery or illness, cushingoid facies, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of latent diabetes mellitus	Not known
Nervous system disorders	Insomnia, dizziness, headache, raised intracranial pressure with papilloedema (pseudotumor cerebri) in children, usually after treatment withdrawal; aggravation of epilepsy	Not known
Eye disorders	Glaucoma, papilloedema, posterior subcapsular cataracts, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease, central serous chorioretinopathy	Not known
Infections and Infestations	Increases susceptibility to, and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis (see 'Special warnings and special precautions for use')	Not known
Blood and Lymphatic system disorders	Leucocytosis	Not known
Immune system disorders	Hypersensitivity including anaphylaxis	Not known
Vascular disorders	Thromboembolism, hypertension	Not known
General disorders and administration site conditions	Fatigue, malaise, impaired healing	Not known
Reproductive system and breast disorders	Menstrual irregularity, amenorrhoea	Not known
Psychiatric disorders	Euphoria, psychological dependence, depression, aggravation of schizophrenia	Not known
Ear and labyrinth disorders	Vertigo	Not known
Investigations	Increased intra-ocular pressure	Not known
Scleroderma renal crisis	Amongst the different subpopulations the occurrence of scleroderma renal crisis varies. The highest risk has been reported in patients with diffuse systemic sclerosis. The lowest risk has been reported in patients with limited systemic sclerosis (2%) and juvenile onset systemic sclerosis (1%).	Not known

**Withdrawal symptoms:** Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see 'Special warnings and special precautions for use' and 'Posology and method of administration'). 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.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

## 4.9 Overdose

Reports of acute toxicity and/or death following overdosage of glucocorticoids are rare. No specific antidote is available; treatment is supportive and symptomatic. Serum electrolytes should be monitored.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogues such as prednisolone are primarily used for their potent anti-inflammatory effect 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

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.

Although peak plasma prednisolone levels are somewhat lower after administration of Deltacortril Enteric and absorption is delayed, total absorption and bioavailability are the same as after plain prednisolone. 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.

Prednisolone is metabolised primarily 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.

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

## 5.3 Preclinical safety data

None stated.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

### **Core:**

Calcium carbonate  
Lactose  
Magnesium stearate  
Maize starch

### **5mg Coating:**

Polyvinyl alcohol  
Titanium dioxide (E171)  
Purified talc  
Lecithin  
Xanthan gum (E415)  
Polyvinyl acetate phthalate  
Polyethylene glycol  
Sodium hydrogen carbonate  
Triethyl citrate  
Purified stearic acid  
Sodium alginate (E401)  
Colloidal silicon dioxide  
Lactose monohydrate  
Methylcellulose (E461)  
Sodium carboxymethyl cellulose  
Carmine (E120)  
Indigo carmine aluminium lake (E132)  
Beeswax (E901)

Carnauba wax (E903)  
Polysorbate 20 (E432)  
Sorbic acid (E200)

## **6.2 Incompatibilities**

Not applicable.

## **6.3 Shelf life**

3 years.

## **6.4 Special precautions for storage**

Do not store above 25°C.

## **6.5 Nature and contents of container**

HDPE container with polypropylene child-resistant tamper evident screw cap containing 30 or 100 tablets.

Not all pack sizes may be marketed.

## **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements.

## **7 MARKETING AUTHORISATION HOLDER**

Phoenix Labs  
Suite 12, Bunkilla Plaza  
Bracetown Business Park  
Clonee  
Co. Meath.  
Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA1113/003/001

## **10 DATE OF REVISION OF THE TEXT**

June 2021