SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Deltacortril 1 mg Gastro-resistant Tablets

Prednisolone 1 mg Gastro-resistant Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1mg of Prednisolone.

Excipients: also includes lactose (33.80mg).

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant Tablets

Yellow, round biconvex gastro-resistant tablets of approximately 6.8mm in diameter.

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 Gastro-resistant Tablets 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 Section 4.4 '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 Section 4.4 'Special warnings and special precautions for use' and Section 4.8 'Undesirable effects')

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

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

Intermittent dosage regimen A single dose of Gastro-resistant 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.

Special populations

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').

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 Section 4.4 'Special warnings and special precautions for use' and Section 4.8 ‘Undesirable effects’). Alternate day dosage is preferable where possible.

4.3 Contraindications

- Hypersensitivity to prednisolone or any of the excipients (see Section 6.1 List of Excipients).
- Systemic infections unless specific anti-infective therapy is employed.
- Ocular herpes simplex because of possible perforation.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 Undesirable effects). 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 Interaction with other medicinal products and other forms of interaction), 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.

Tumorigenicity: direct tumour-inducing effects of the glucocorticoids are not known, but the particular risk that malignancies in patients undergoing immunosuppression with these or other drugs will spread more rapidly is a well-recognised problem (see Section 4.5 Interaction with other medicinal products and other forms of interaction).

Calciphylaxis may occur very rarely during treatment with corticosteroids (see section 4.8 Undesirable effects). Although calciphylaxis is most commonly observed in patients who have end stage kidney failure, it has also been reported in patients taking corticosteroids who have minimal or no renal impairment and normal calcium, phosphate and parathyroid hormone levels. Patients/carers should be advised to seek medical advice if symptoms develop.

Caution is necessary when oral corticosteroids, including Deltacortril Gastro-resistant Tablets, 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.

- Inflammatory bowel disease: Symptoms recurred in a patient with Crohn's disease on changing from conventional to enteric-coated tablets of prednisolone. This was not an isolated occurrence in the author's unit, and it was advocated that only non-enteric coated prednisolone tablets should be used in Crohn's disease, and that the enteric coated form should be used with caution in any condition characterized by diarrhoea or a rapid transit time.

- Hypertension.

- Congestive heart failure.

- Liver failure.

- Hepatic disease: In patients with acute and active hepatitis, protein binding of the glucocorticoids will be reduced and peak concentrations of administered glucocorticoids increased. Elimination of prednisolone will also be impaired. There is an enhanced effect of corticosteroids in patients with cirrhosis.

- 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.

- Corticosteroid requirements may be reduced in menopausal and post-menopausal women.

- 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.

- Duchenne's muscular dystrophy: transient rhabdomyolysis and myoglobinuria may occur following strenuous physical activity. It is not known whether this is due to prednisolone itself or the increased physical activity.

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 titrate the dose appropriately against disease activity (see Section 4.2 '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 reinstituted. 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.

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 ’Interaction with other medicinal products and other forms on interaction’).

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.

Systemic glucocorticoid treatment can cause severe exacerbation of bullous exudative retinal detachment and lasting visual loss in some patients with idiopathic central serous chorioretinopathy (See Section 4.8 ‘Undesirable effects’).

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.

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 (see Section 4.8 ‘Undesirable effects’).

Raised intracranial pressure Raised intracranial pressure with papilloedema (pseudotumour cerebri) associated with corticosteroid treatment has been reported in both children and adults. The onset usually occurs after treatment withdrawal (See section 4.8 ‘Undesirable effects’).

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 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.

There is an increased risk of nuclear cataracts (see Section 4.8 ‘Undesirable Effects).

4.5 Interaction with other medicinal products and other forms of interaction

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

Antacids	The absorption of prednisolone may be reduced by large doses of some antacids such as magnesium trisilicate or aluminium hydroxide.
Antibacterials	Rifamycins accelerate metabolism of corticosteroids and thus may reduce their effect. Erythromycin inhibits metabolism of methylprednisolone and possibly other corticosteroids. Prednisolone can lower plasma levels of isoniazid. Where a reduced response during concurrent use is noted, dosage adjustment of isoniazid may be necessary.
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.
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.
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.
Antimuscarinics (Anticholinergics)	Prednisolone has been shown to have antimuscarinic activity. If used in combination with another antimuscarinic drug could cause impairment to memory and attention in the elderly.
Antithyroids	Prednisolone clearance increased by the use of carbimazole and thiamazole.
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.
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 Gastro-resistant 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.
Hormonal contraceptives	Oral contraceptives increased prednisolone concentrations by 131%. May increase AUC and reduce clearance in oral contraceptives containing ethinylestradiol, mestranol, desogestrel, levonorgestrel, norgestrel or norethisterone.
Immunosuppressants	Tumorigenicity: direct tumour-inducing effects of the glucocorticoids are not known, but the particular risk that malignancies in patients undergoing immunosuppression with these or other drugs will spread more rapidly is a well-recognised problem.
Liquorice	Glycyrrhizin can delay the clearance of prednisolone
Mifepristone	Effect of corticosteroids may be reduced for 3-4 days after mifepristone
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.
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.
Protease inhibitors	Ritonavir possibly increases plasma concentrations of prednisolone and other corticosteroids by reduction in clearance of prednisolone through the inhibition of P450 isoenzyme CYP3A4.
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.
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.

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.

The concentration of the steroid in the milk can be between 5 and 25% of those in the serum and the two roughly parallel one another after an oral dose.

There are no reports found regarding neonatal toxicity following exposure to corticosteroids during lactation, however if maternal doses >40mg/day of prednisolone is prescribed, the infant should be monitored for adrenal suppression.

4.7 Effects on ability to drive and use machines

The effect of Deltacortril Gastro-resistant Tablets 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

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.
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 'Special warnings and special precautions for use').
Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:
Very common: ≥1/10
Common: ≥1/100 to <1/10
Uncommon: ≥1/1,000 to <1/100
Rare: ≥1/10,000 to <1/1,000
Very rare: <1/10,000

Not known: cannot be estimated from the available data

System Organ Class	Frequency	Undesirable Effect
Infections and Infestations	Not known	Increases susceptibility to, and severity of infections[1], opportunistic infections, recurrence of dormant tuberculosis[2], oesophageal candidiasis.
Blood and lymphatic system disorders	Not known	Leucocytosis.
Immune system disorders	Not known	Hypersensitivity including anaphylaxis, Scleroderma renal crisis[10].
Endocrine disorders	Not known	Suppression of the hypothalamo-pituitary adrenal axis[3], cushingoid facies, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of latent diabetes mellitus.
Metabolism and nutrition disorders	Not known	Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen and calcium balance, glucose intolerance and protein catabolism. Increase both high and low density lipoprotein cholesterol concentration in the blood. Increased appetite[4]. Weight gain, obesity, hyperglycaemia, dyslipidaemia.
	Very rare	Calciphylaxis[5]
Psychiatric disorders	Common	Irritability, depressed and labile mood, suicidal thoughts, psychotic reactions, mania, delusions, hallucinations, and aggravation of schizophrenia. behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia.
	Not known	Euphoria, psychological dependence, depression.
Nervous system disorders	Not known	Depression, insomnia, dizziness, headache, vertigo. Raised intracranial pressure with papilloedema (pseudotumor cerebri)[6]. Aggravation of epilepsy, epidural lipomatosis. vertebrobasilar stroke[7]
Eye disorders	Not known	Glaucoma, papilloedema, posterior subcapsular cataracts, nuclear cataracts (particularly in children), exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease**.** Severe exacerbation of bullous exudative retinal detachment; lasting visual loss in some patients with idiopathic central serous chorioretinopathy.[8]
Ear and labyrinth disorders	Not known	Vertigo.
Cardiac disorders	Not known	Congestive heart failure in susceptible patients, hypertension, increased risk of heart

		failure.Increased risk of cardiovascular disease, including myocardial infarction.[9]
Vascular disorders	Not known	Thromboembolism.
Gastrointestinal disorders	Not known	Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, diarrhoea, oesophageal ulceration, acute pancreatitis.
Skin and subcutaneous tissue disorders	Not known	Hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, pruritis, rash, urticaria.
Musculoskeletal and connective tissue disorders	Not known	Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, tendinopathies (particularly of the Achilles and patellar tendons), myalgia, growth suppression in infancy, childhood and adolescence.
Reproductive system and breast disorders	Not known	Menstrual irregularity, amenorrhoea.
General disorders and administration site conditions	Not known	Fatigue, malaise, impaired healing
Investigations	Not known	Increased intra-ocular pressure, may suppress reactions to skin tests.

[1.] with suppression of clinical symptoms and signs.
[2.] see Section 4.4 ‘Special warnings and precautions for use’.
[3.] particularly in times of stress, as in trauma, surgery or illness.
[4.] which may result in weight gain
[5.] see Section 4.4 ‘Special warnings and precautions for use’.
[6]. usually after treatment withdrawal
[7]. exacerbation of giant cell arteritis, with clinical signs of evolving stroke has been attributed to prednisolone.
[8]. see Section 4.4 ‘Special warnings and precautions for use’
[9]. with high dose therapy
[10.] 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 'Special warnings and special precautions for use' and Section 4.2 '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. Psychological effects have been reported on withdrawal of corticosteroids.

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.

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.

High systemic doses of corticosteroids caused by chronic use have been associated with adverse effects such as neuropsychiatric disorders (psychosis, depression, hallucinations), cardiac dysrhythmias and Cushing's syndrome.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use.

ATC code: H02AB06

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

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 Gastro-resistant Tablets 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.

Significant differences in the pharmacokinetics of prednisolone amongst menopausal women have been described. The postmenopausal women had reduced unbound clearance (30%), reduced total clearance and increased half-life of prednisolone.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:

calcium carbonate

lactose monohydrate

magnesium stearate

maize starch

Coating Preparation:

Sub-coat:

Polyvinyl alcohol

Titanium dioxide (E171)

Talc
Lecithin (soya)
Xanthan gum (E415)

Gastro-resistant coat:
Polydimethylsiloxane
Polyethylene glycol sorbitan tristearate
Methylcellulose
Silica gel
Polyethylene glycol stearate
Sorbic acid
Benzoic acid (E210)
Sulfuric acid
Polyvinyl acetate phthalate
Titanium dioxide (E171)
Talc
Macrogol 4000,
Sodium hydrogen carbonate
Triethyl citrate
Purified stearic acid,
Sodium alginate (E401)
Colloidal anhydrous silica

Coloured top coat:
Lactose monohydrate
Methylcellulose (E461)
Macrogol / PEG 4000
Titanium dioxide (E171)
Sodium carboxymethylcellulose
Iron oxide yellow (E172)

Polish:
White beeswax (E901)
Carnauba wax (E903)
Polysorbate 20 (E432)
Sorbic acid (E200)

6.2 Incompatibilities

None.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container to protect from moisture.

6.5 Nature and contents of container

White HDPE bottles with a white polypropylene child resistant, tamper evident screw cap, pack size 100 tablets.

Aluminium /aluminium blister strips in a cardboard carton, pack size 30 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 35104/0028

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/01/2025

10 DATE OF REVISION OF THE TEXT

23/01/2025