Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Prednisolone Renata 5 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains prednisolone 5 mg.

Excipient(s) with known effect
77.80 mg lactose (anhydrous).
0.0675 mg sodium benzoate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

Round-shaped, white tablets of 6.35 mm in diameter debossed with 'P' on one side and breakline on the other side.
The scoreline is not intended for breaking the tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nonspecific therapy in conditions where the anti-inflammatory and immunosuppressive action of prednisolone is desirable. Examples include rheumatoid arthritis, systemic lupus erythematosus, some vasculitis such as temporal arteritis and polyarteritis nodosa, sarcoidosis, asthma bronchial, ulcerative colitis, haemolytic anaemia and granulocytopenia, and severe allergic conditions.

In tumour treatment, in some cases of acute leukaemia, lymphoma and prostate cancer.

4.2 Posology and method of administration

Posology
Individual. Generally 10-30 mg daily. In very severe acute cases, may up to 50-60 mg or more be given for a few days. When satisfactory efficacy is achieved, the daily dose is reduced by 2.5-5 mg every other to every five days (at the highest doses more rapidly) to the minimum possible maintenance dose. This should preferably not exceed 10 mg/day.

If the entire maintenance dosage is given in the morning (at 8 a.m.), prednisolone will act in line with the natural circadian rhythm of the adrenal cortex and results in minimal adrenal cortex inhibition. This dosage type can generally be tested as a starting point; however, in some cases, e.g. for rheumatics with pronounced morning stiffness and for asthmatics who need corticosteroid protection during the night, a late evening dose or split dosage may be preferable.

In some cases of asthma, allergic conditions, dermatoses, etc., giving a double daily dose as a single dose once every other day in the morning will be advantageous.

Discontinuation of the dose should be gradual since the own ACTH secretion may be reduced after prolonged treatment.

Increased dose may be given before, during and after stress situations.

Increased dose in case of fever and stress.

Increased insulin dose should be given to diabetics during cortisone treatment.

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 precautions for use'). Alternate day dosage is preferable where possible.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Systemic fungal infection.

Administration of live vaccines is contraindicated in patients receiving corticosteroids in immunosuppressive doses.

In those conditions where prednisolone treatment can save lives, none of the contraindications generally apply.

4.4 Special warnings and precautions for use

As the complications of glucocorticoid treatment depend on the dose and duration of treatment, a risk/benefit assessment must be made in each case regarding dose and duration of treatment, and whether daily or intermittent treatment should be used.

The lowest possible corticosteroid dose needed to control the disease being treated should be used. When dosage reduction is possible, this should be done gradually.

Immunosuppressive effects / increased susceptibility to infection
Glucocorticoids, including prednisolone, may increase susceptibility to infection, mask symptoms of infection, and new infections may occur during treatment.

Infections caused by viruses, bacteria, fungi, protozoa, or intestinal worms may be associated with the use of corticosteroids alone or corticosteroids in combination with other immunosuppressants that affect cellular immunity, humoral immunity, or neutrophil function. Infections can be mild, but also severe and in some cases fatal. The risk of infectious complications increases with increased dose.

Glucocorticoids should not be given in infections without concomitant causal therapy.

Chickenpox and measles can have a more serious or even fatal course in non-immunised children and adults treated with corticosteroids. Children, or adults who have not had these diseases, and who are taking immunosuppressive doses of corticosteroids, should be advised to avoid exposure to chickenpox and measles, and to seek medical attention if exposed.

The use of prednisolone in active tuberculosis should be limited to those cases of fulminant or disseminated tuberculosis where the corticosteroid is used for the treatment of the disease in combination with appropriate tuberculosis therapy. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close monitoring is necessary as the disease may be reactivated. In case of prolonged corticosteroid treatment, these patients should receive tuberculosis prophylaxis

High dosage of corticosteroids may interfere with active immunisation. Vaccination with live vaccines should be carried out under close supervision and not in patients on long-term treatment with corticosteroids in immunosuppressive doses.

Immune system disorders
As rare cases of skin reactions and anaphylactic/anaphylactoid reactions have occurred in patients treated with corticosteroids, appropriate precautions should be taken prior to administration, particularly if the patient has had a previous allergic reaction to any medicinal product.

Endocrine disorders
Long-term treatment with pharmacological doses of corticosteroid may lead to secondary adrenal cortex insufficiency. The risk may be reduced by giving the treatment every other day (see section 4.2).

Patients receiving maintenance corticosteroid therapy who are under unusual stress (e.g. infection, surgery, or trauma) require higher corticosteroid doses before, during, and after the stressful situation.

Abrupt discontinuation of treatment may lead to acute adrenal cortex insufficiency, which may be fatal. The risk of secondary adrenal cortex insufficiency may be reduced by gradual dose reduction. This type of relative insufficiency may persist for months after the treatment has ended, so hormone therapy should be reinitiated in stressful situations that occur during this time period. Since excretion of mineralocorticoids may be impaired, salts and/or mineralocorticoids should be administered concomitantly.

A "steroid withdrawal syndrome", apparently unrelated to adrenal cortex insufficiency, may also occur after abrupt discontinuation of glucocorticoids. This syndrome presents with symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss and/or hypotension. These effects are thought to be due to the sudden change in glucocorticosteroid concentration rather than low corticosteroid levels.

Patients with hypothyroidism or liver cirrhosis have an enhanced effect of corticosteroids.

Pheochromocytoma-related crisis, which may be fatal, has been reported following administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after consideration of individual risk / benefit.

Metabolism and nutrition disorders
Corticosteroids, including prednisolone, may increase blood sugar levels, aggravate pre-existing diabetes and increase the risk of developing diabetes in patients on long-term corticosteroids.

Mental disorders
Potentially serious mental disorders may occur during treatment with corticosteroids, including prednisolone. These can range from euphoria, sleep disturbances, mood swings, personality changes and severe depression to psychotic manifestations. In addition, pre-existing emotional instability and psychotic tendencies may be aggravated by corticosteroids (see section 4.8). Symptoms typically start within a few days or weeks of starting treatment.

Most reactions will be reduced after dose reduction or discontinuation, but specific treatment may be necessary.

Mental effects have been reported with discontinuation of corticosteroids, the frequency is unknown. Patients/carers should be advised to seek medical attention if the patient experiences mental symptoms, especially if depression or suicidal thoughts are suspected. Patients/carers should be aware that mental disorders may occur either during or immediately after dose tapering / discontinuation of systemic steroids.

Nervous system disorders
Corticosteroids should be used with caution in patients with seizure disorders.

Cardiac disorders
Adverse reactions of glucocorticoids on the cardiovascular system, such as dyslipidaemia and hypertension, may predispose treated patients with pre-existing cardiovascular risk factors for additional cardiovascular events at high doses and prolonged duration of treatment. Corticosteroids should therefore be initiated in these patients only after careful consideration, and risk modifying measures and additional cardiac monitoring considered if necessary. Low dose and treatment every other day may reduce the complications of treatment with corticosteroids.

Vascular disorders
As cortisone has been reported to increase blood clotting tendency in rare cases and thus could accelerate the development of intravascular thrombosis, thromboembolism and thrombophlebitis, corticosteroids should be used with caution in patients with thromboembolic diseases.

Gastrointestinal disorders
High doses of corticosteroids may cause acute pancreatitis.

There are no unambiguous data that establish that corticosteroids cause stomach ulcers. Glucocorticoid therapy may mask peritonitis and other signs and symptoms associated with gastrointestinal conditions such as perforation, obstruction, or pancreatitis. In combination with NSAIDs, the risk of gastrointestinal ulcers is increased.

Corticosteroids should therefore be used with caution in non-specific ulcerative colitis if there is a likelihood of impending perforation, abscess or other pyogenic infection, diverticulitis, recent anastomoses, or active or latent peptic ulcer.

Hepatobiliary disorders
Diseases of the liver and biliary tract have been reported in rare cases and in the majority of these cases the condition was reversible after discontinuation of treatment. Appropriate monitoring measures are required.

Musculoskeletal disorders
Acute myopathy has been reported with high corticosteroid doses, most commonly in patients with neuromuscular transmission disorders (e.g. myasthenia gravis), or in patients concomitantly treated with anticholinergics, e.g. neuromuscular blocking medicinal products (such as pancuronium) (see section 4.5). This acute myopathy is generalised, may involve eye and respiratory muscles, and may lead to tetraparesis. Increased creatine kinase may occur. Clinical improvement or recovery after discontinuation of corticosteroids may take weeks or years.

Corticosteroids should be used with caution in patients with osteoporosis.

Renal and urinary disorders
Corticosteroids should be used with caution in patients with renal insufficiency.

Acute kidney crisis (renal crisis in scleroderma)
Caution is required in patients with systemic sclerosis because an increased incidence of (possibly fatal) renal crisis in scleroderma, with hypertension and reduced urine production, has been observed at a daily prednisolone dose of 15 mg or more. Therefore, blood pressure and renal function (S-creatinine) should be routinely monitored. In case of suspected renal crisis, blood pressure should be carefully monitored.

Impact on electrolytes and fluid balance
Systemic corticosteroids should be used with caution in patients with heart failure or hypertension. Medium and high doses of hydrocortisone or cortisone may lead to increased blood pressure, salt and water retention, and increased potassium excretion. These effects are less likely with synthetic derivatives, except when used in high doses. Dietary restrictions with lower salt intake as well as potassium supplements may be necessary.

All corticosteroids increase calcium excretion.

Eye disorders
Visual disturbance may be reported with systemic and topical use of corticosteroids. If a patient presents with symptoms such as blurred vision or other visual disturbances, consider referring the patient to an ophthalmologist for investigation of possible causes. These may include cataracts, glaucoma, or rare diseases such as central serous chorioretinopathy (CSCR), which have been reported following the use of systemic and topical corticosteroids.

Tumour lysis syndrome (TLS)
Tumour lysis syndrome (TLS) has been reported post-marketing in patients with malignancies, including haematological malignancies and solid tumours, following use of systemic corticosteroids alone or in combination with other cytostatic medicines. Patients at high risk for TLS, such as patients with tumours that have a high cell division rate, high tumour burden, and high sensitivity to cytotoxic agents, should be closely monitored and appropriate precautions taken.

Use for children
Corticosteroids cause growth inhibition in infants, children and adolescents, so long-term treatment with pharmacological doses should be avoided. If long-term treatment is required, the growth and development of the infant/child should be closely monitored (see section 4.2).

Infants and children on long-term corticosteroid therapy are at particular risk of developing elevated intracranial pressure.

Excipients
This medicinal product contains lactose. Patients with rare hereditary problems such as galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicinal product.

This medicinal product contains sodium benzoate. Increase in bilirubinaemia following its displacement from albumin may increase neonatal jaundice which may develop into kernicterus (non-conjugated bilirubin deposits in the brain tissue).

4.5 Interaction with other medicinal products and other forms of interaction

The following combinations of Prednisolone may require dose adjustment.

Phenobarbital, Phenytoin, Carbamazepine: Phenobarbital (which is also a metabolite to primidone), Phenytoin and Carbamazepine separately and in combination induces the metabolism of hydrocortisone, prednisolone and methylprednisolone (shown in children with asthma) resulting in increased dose requirements. The interaction is likely to apply to the entire group of glucocorticoids.

Non-steroidal anti-inflammatory agents:

1) The incidence of gastrointestinal bleeding and ulceration may be increased if corticosteroids are given with NSAIDs.

2) Corticosteroids may increase clearance of high doses of acetylsalicylic acid, which may lead to lower serum salicylate levels. Upon discontinuation of corticosteroid therapy, serum salicylate levels may rise, which could lead to an increased risk of toxic effects of salicylate.

Medical products for diabetes: Glucocorticoids increase blood sugar levels. Patients with diabetes mellitus receiving concomitant insulin and/or oral hypoglycaemic agents may need to adjust the doses of such therapy.

Oestrogens (including oral contraceptives containing oestrogens): Oestrogens increase the concentration of transcortin. The effect of glucocorticoids binding to transcortin may be enhanced and dose adjustments may be needed if oestrogens are added to or removed from a stable treatment regimen.

Potassium reducing agent: Potassium-reducing diuretics (e.g. thiazides, furosemide, etacrynic acid) and other medicinal products that reduce the amount of potassium such as amphotericin B, xanthines and beta2-agonists may enhance the potassium-lowering effect of glucocorticoids. Serum potassium should be closely monitored in patients receiving glucocorticoids and potassium reducing agents.

Rifampicin: Rifampicin induces the microsomal oxidation of glucocorticoids (hydrocortisone, prednisolone, methylprednisolone). This leads to an increased steroid requirement during rifampicin treatment and reduced steroid requirement after such treatment.

Isoniazid : Prednisolone also has a potential effect that involves increased acetylation rate and clearance of isoniazid.

Oral anticoagulants: There are reports of changes in the effect of anticoagulants given at the same time as prednisolone. Prothrombin time (INR) should be followed during treatment.

CYP3A-inhibitors, including medical products containing cobicistat: These are expected to increase the risk of systemic adverse reactions. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side effects, and if so, patients should be monitored for systemic adverse reactions from corticosteroids.

Anticholinergics, neuromuscular blockers: Corticosteroids may affect the effect of anticholinergics.

1) Acute myopathy has been reported with concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blockers (see section 4.4).

2) Antagonism with the neuromuscular blocking effect of pancuronium and vecuronium has been reported in patients taking glucocorticosteroids. This interaction can be expected with any competitive neuromuscular blocker.

Anticholinesterases: Interaction between glucocorticoids and anticholinesterases such as ambenonium, neostigmine and pyridostigmine can lead to significant weakness in people with myasthenia gravis. If possible, anticholinesterase therapy should be discontinued at least 24 hours prior to initiating glucocorticoid therapy.

Concomitant use with methotrexate may increase the risk of haematological toxicity.

4.6 Fertility, pregnancy and lactation

Pregnancy

In animal studies, corticosteroids have been shown to cause various malformations (cleft palate, skeletal malformations, see section 5.3). The relevance for humans is unknown. After long-term treatment, reduced placental and birth weight has been

found in humans and animals. In addition, with long-term treatment there is a risk of adrenal insufficiency in the newborn. Therefore, during pregnancy, corticosteroids should be given after special consideration.

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

Breast-feeding
Prednisolone passes into breast milk, but the risk of affecting the baby appears unlikely with therapeutic doses.

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

4.7 Effects on ability to drive and use machines

The effect of corticosteroids on the ability to drive and use machines has not been systematically investigated. Adverse reactions such as dizziness, visual disturbances and fatigue are possible after treatment with corticosteroids. In the event of such adverse reactions, the patient should not drive or use machines.

4.8 Undesirable effects

Apart from substitution therapy, corticosteroid treatment always involves an overdose compared to the physiological condition. Adverse reactions occur mainly in long-term treatment but also depend on dose size as well as individual sensitivity.

The following side adverse reactions have been observed and reported during treatment with Prednisolone with the following frequencies: Very common (≥1/10), common (≥1/100 to <1/10) uncommon (≥1/1 000 to <1/100), rare (≥1/10 000 to <1/1 000), very rare (<1/10 000), not known (cannot be estimated from the available data).

Organ system	**Very common ≥ 1/10**	**Common ≥ 1/100, < 1/10**	**Uncommon ≥ 1/1 000, < 1/100**	**Rare ≥ 1/10 000, < 1/1 000**	**Very rare <1/10 000**	**Not known (cannot be estimated from available data)**
Infections and infestations		Opportunistic infection Activation of infection (e.g. tuberculosis)				
Blood and lymphatic system disorders						Leucocytosis (due to intravascular granulocyte redistribution)
Immune system disorders						Drug hypersensitivity Anaphylactic reaction Anaphylactoid reaction
Endocrine disorders		Hypothalamus pituitary adrenal gland (HPA) axis inhibition, Cushing-like symptoms. Growth inhibition (in children).				Steroid withdrawal syndrome (see section 4.4) Pheochromocytoma-related crisis (see section 4.4).
Metabolism and nutrition disorders		Hypokalaemia Sodium retention Increased gluconeogenesis Catabolic effects Osteoporosis				Metabolic acidosis Fluid retention Hypokalaemic alkalosis Dyslipidaemia Decreased glucose tolerance (diabetes mellitus may deteriorate and latent diabetes may manifest) Lipomatosis Increased appetite (which may lead to

						weight gain)
Mental disorders			Activation of previous mental disorders (high dose)	Depression, mania in patients without a previously known mental illness		Affective disorder (includes euphoria, affective lability, drug dependence, suicidal thoughts) Psychotic disorder (includes delusions, hallucinations, and schizophrenia) Psychological disorder Personality change Confusional state Anxiety Mood swings Abnormal behaviour Insomnia Irritability
Nervous system disorders				Benign intracranial hypertension		Epidural lipomatosis Seizures Amnesia Cognitive disorder Dizziness Headache
Eye disorders			Cataract Glaucoma			Central serous chorioretinopathy (see section 4.4) Exophthalmos blurred vision (see section 4.4)
Cardiac disorders						Heart failure (in sensitive patients) Bradycardia*
Vascular disorders		Oedema Hypertension				Thromboembolic events
Respiratory, thoracic and mediastinal disorders						Hiccough
Gastrointestinal disorders						Peptic ulcer (possibly with perforation and bleeding) Bowel perforation Pancreatitis Ulcerative oesophagitis Abdominal distension Abdominal pain Diarrhoea Dyspepsia Nausea
Skin and subcutaneous tissue disorders		Skin atrophy Impaired wound healing				Angioedema Hirsutism Petechiae Ecchymosis Erythema Hyperhidrosis Striae Itching Urticaria Acne
Musculoskeletal and connective tissue disorders		Muscle atrophy		Aseptic bone necrosis Tendon rupture		Muscle weakness Myalgia Myopathy Pathological fracture Neuropathic arthropathy Arthralgia
Renal and urinary disorders						Acute kidney crisis (renal crisis in scleroderma)**
Reproductive system and breast disorders						Irregular menstruations
General disorders and administration site conditions						Fatigue Feeling sick
Investigations						Increased calcium amounts in urine Increased alanine amino transferase Increased aspartate amino transferase Blood alkaline phosphatase

						increased Blood urea Suppression of skin test reactions[1]

[1] Not a MedDRA term.
*At high doses.
**Acute renal crisis (scleroderma renal crisis)
The incidence of acute renal crisis varies between the different subpopulations. The greatest risk has been reported in patients with diffuse systemic sclerosis. The smallest risk has been reported in patients with limited systemic sclerosis (2%) and systemic sclerosis with juvenile onset (1%).

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. Website: www.hpra.ie.

4.9 Overdose

Reports of acute toxicity and/or death following overdose of glucocorticoids are rare. Possibly, acute overdose may aggravate pre-existing conditions such as ulcer, electrolyte disturbances, infections and oedema.

Treatment : Usually not required. If justified gastric emptying, charcoal. In the event of overdose, there is no specific antidote, but the treatment is supportive and symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glucocorticoid, ATC code: H02AB06.

Synthetic glucocorticoid with anti-inflammatory, immunosuppressive and anti-allergic effect. Prednisolone has a 4-5 times higher anti-inflammatory effect per unit weight than cortisone but affects electrolyte metabolism to a lesser extent. The mechanism of effect is not fully understood yet.

5.2 Pharmacokinetic properties

Absorption
Prednisolone is rapidly absorbed into the gastrointestinal tract when given orally. Maximum plasma concentration is reached after 1 to 2 hours after oral administration. The plasma half-life is normally 2 to 4 hours. Its initial absorption, but not the total bioavailability, is affected by food.

Distribution
Prednisolone is highly bound to plasma proteins and has high affinity to transcortin. Volume of distribution and clearance are reported to increase when switching from low to medium doses.

Biotransformation
Prednisolone is primarily metabolised in the liver to a biologically inactive compound. Prednisolone can be reversibly converted to prednisone by 11β-hydroxysteroid dehydrogenase.

The absolute biological availability of prednisolone is on average 82% compared to intravenously administered prednisolone after a single dose of 10 mg. At normal dosing, the duration of effect is calculated to be 12-36 hours.

Elimination
Prednisolone is excreted in the urine as free and conjugated metabolites, together with small amounts of unchanged prednisolone. More than 90% of the given amount is excreted in the urine. 7-15% is excreted in unchanged form.

5.3 Preclinical safety data

In animal studies, corticosteroids have been shown to cause various types of malformations (cleft palate, skeletal malformations). After long-term treatment, a reduced placental and birth weight has been found in animals.

Corticosteroids have been shown to reduce fertility when administered to rats.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose (Anhydrous)
Crospovidone (Type A)
Docusate Sodium/Sodium Benzoate
Silica, Colloidal Anhydrous
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

For HDPE Bottle: 3 years.
For Blister (Alu-PVC; Alu-PVDC): 2 years.

6.4 Special precautions for storage

For HDPE Bottle: This medicinal product does not require any special storage conditions.
For Blister (Alu-PVC; Alu-PVDC): Do not store above 25°C.

6.5 Nature and contents of container

Aluminium-PVC or Aluminium-PVC/PE/PVDC blister packs containing 28, 56, 98 or 112 tablets.

HDPE bottles with Child-resistant closure with silica-gel canister containing 25 tablets.
The canister containing the desiccant is not meant to be consumed.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Renata Pharmaceuticals (Ireland) Limited
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A91 NN29
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22865/021/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th of August 2026

10 DATE OF REVISION OF THE TEXT