1.3.1.1. PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

LENISOLONE TABLETS 5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of LENISOLONE TABLETS contains 5 mg prednisolone.

Contains sugar: Lactose monohydrate 72,00 mg

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets.

LENISOLONE TABLETS is a white shallow biconvex tablet bisected on one side plain on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

LENISOLONE TABLETS is indicated in all conditions where corticosteroid therapy is likely to be of benefit. These include:

- Acute haemolytic disorders,
- Allergic disorders,
- Asthma,
- Leukaemia,
- Thrombocytopenic purpura,

- Celiac disease,
- Insulin resistance in diabetes mellitus,
- Immunosuppression,
- Liver disorders,
- Ulcerative colitis.

4.2. Posology and method of administration

Posology

Adults

The usual dose is up to 60 mg daily in divided doses.

LENISOLONE TABLETS withdrawal should always be gradual. The rate depends on the patient's response, the dose and duration of therapy. Adrenal function should be monitored throughout withdrawal and symptoms attributable to overrapid withdrawal should be countered by resuming a higher dose and continuing the reduction at a slower rate.

Paediatric population

No data are available

Method of administration

Tablets for oral administration.

4.3. Contraindications

LENISOLONE TABLETS is contraindicated in:

- Patients with hypersensitivity to prednisolone or to any excipients in LENISOLONE TABLETS (see section 6.1).
- Patients with peptic ulcer.
- Patients with osteoporosis (see section 4.4).

- Patients with psychoses or severe psychoneuroses (see section 4.4).
- Patients with active tuberculosis or doubtfully quiescent tuberculosis (see section 4.4).
- Patients with acute infection including Herpes zoster and Herpes simplex ulceration of the eye (see section 4.4).
- Vaccination with live vaccine (killed vaccines or toxoids may be given) (see section 4.4).

4.4. Special warnings and precautions for use

General

Caution and frequent patient monitoring is necessary when oral corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, are prescribed in patients with the following conditions:

- Hypertension,
- Congestive heart failure,
- Diabetes mellitus or in those with a family history of diabetes,
- Chronic renal failure, uraemia, renal insufficiency,
- Liver failure,
- Hepatic disease: In patients with acute and active hepatitis, protein binding of the glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, will be reduced and peak concentrations increased. Elimination of prednisolone, as in LENISOLONE TABLETS, will also be impaired. There is an enhanced effect of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, in patients with cirrhosis,

- Menopause, post-menopause: Corticosteroid requirements, such as prednisolone, as in LENISOLONE TABLETS, 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. Existing emotional instability or psychotic tendencies may be aggravated by corticosteroids including prednisolone as in LENISOLONE TABLETS (see section 4.3),
- Epilepsy, and/or seizure disorders,
- Previous steroid myopathy,
- Myasthenia gravis: Glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy,
- Thromboembolic disorders: cortisone, such as prednisolone, as in LENISOLONE TABLETS, has been reported to increase blood coagulability and to precipitate intravascular thrombosis, thromboembolism, and thrombophlebitis; corticosteroids, such as prednisolone, as in LENISOLONE TABLETS should be used with caution in patients with thromboembolic disorders.

Risk of bradycardia

Bradycardia is rare but serious adverse effect of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, that may be both symptomatic and asymptomatic. It is most likely to occur with high doses of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, however, bradycardia can occur even with standard doses of oral corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, and is reversible with dose reduction or discontinuation.

Furthermore, patients with pre-existing cardiac or renal problems or electrolyte imbalance are at high risk of experiencing bradycardia (see section 4.8).
The degree of risk may be increased by the concomitant use of other medicines that causes bradycardia as an adverse event.

Pheochromocytoma Crisis

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids, as in LENISOLONE TABLETS should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Duchenne muscular dystrophy

Transient rhabdomyolysis and myoglobinuria may occur following strenuous physical activity. It is not known whether this is due to prednisolone, as in LENISOLONE TABLETS, 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 or whenever possible as a single morning dose on alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity (see section 4.2).

Psychiatric adverse reactions

Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids, such as prednisolone, as in LENISOLONE TABLETS (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 section 4.5), 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 tampering/withdrawal of systemic steroids, such as prednisolone, as in LENISOLONE TABLETS, although such reactions have been reported infrequently.

Particular care is required when considering the use of systemic corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, 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 (see section 4.3).

Tumorigenicity

Direct tumour-inducing effects of the glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, are not known, but the particular risk that malignancies in patients undergoing immunosuppression with these or other medicines will spread more rapidly is well-recognised (see section 4.5).

Calciphylaxis

Calciphylaxis may occur very rarely during treatment with corticosteroids, such as prednisolone, as in LENISOLONE TABLETS (see section 4.8). Although calciphylaxis is most commonly observed in patients who have end stage kidney failure, it has also been reported in patients taking corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, 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.

Adrenocortical insufficiency

Sudden withdrawal or reduction in dosage, or an increase in corticosteroid requirements associated with the stress of infection, or accidental or surgical trauma may cause acute adrenal insufficiency leading to a fatal outcome. Symptoms of adrenal insufficiency include malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration. Deaths have followed the abrupt withdrawal of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS.

Pharmacologic doses of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, 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 treatment.

Medicine-induced secondary adrenocortical insufficiency may therefore be minimised 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, such as prednisolone, as in LENISOLONE TABLETS, have

been stopped following prolonged therapy they may need to be temporarily re-introduced.

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 infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised when corticosteroids, including prednisolone as in LENISOLONE TABLETS, are used. The immunosuppressive effects of glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, may result in the activation of latent infection or exacerbation of intercurrent infection.

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, such as prednisolone, as in LENISOLONE TABLETS, 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, such as prednisolone, as in LENISOLONE TABLETS, should not be stopped and the dose may need to be increased.

Measles

Patients taking corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs.

Administration of live vaccines

Live vaccines should not be given to individuals on high doses of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, due to impaired immune response. Live vaccines should be postponed until at least 3 months after stopping treatment with LENISOLONE TABLETS (see also section 4.5).

Ocular effects

Prolonged use of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, may produce posterior subcapsular cataracts and nuclear cataracts, 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, such as prednisolone, as in LENISOLONE TABLETS.

Corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, is contraindicated in patients with ocular herpes simplex because of possible perforation (see section 4.3).

LENISOLONE TABLETS should also be used with great caution in the presence of glaucoma.

Systemic glucocorticoid treatment, such as prednisolone, as in LENISOLONE TABLETS, 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).

Cushing's disease

Because glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, can produce or aggravate Cushing's syndrome, glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, should be avoided in patients with Cushing's disease.

There is an enhanced effect of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, in patients with hypothyroidism.

Psychic derangements may appear when corticosteroids, including prednisolone as in LENISOLONE TABLETS, are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations (see section 4.8).

Raised intracranial pressure

Raised intracranial pressure with papilloedema (pseudotumour cerebri) associated with corticosteroid treatment, such as prednisolone, as in LENISOLONE TABLETS, has been reported. The onset usually occurs after treatment withdrawal (see section 4.8).

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, as in LENISOLONE TABLETS. 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, such as prednisolone, as in LENISOLONE TABLETS, 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.

LENISOLONE TABLETS should be used with great caution in elderly patients.

Paediatric population

Corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, cause growth retardation in infancy, childhood and adolescence, which may be irreversible. There is also an increased risk of nuclear cataracts (see section 4.8).

Excipients

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take LENISOLONE TABLETS.

4.5. Interaction with other medicines and other forms of interaction

CYP3A inhibitors

Co-treatment with CYP3A inhibitors, including cobicistat-containing medicines, 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.

Antacids

The absorption of prednisolone, as in LENISOLONE TABLETS, may be reduced by large doses of some antacids such as magnesium trisilicate or aluminium hydroxide.

Antibacterials

Rifamycins accelerate metabolism of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, and thus may reduce their effect. Erythromycin inhibits metabolism of methylprednisolone and possibly other corticosteroids such as prednisolone, as in LENISOLONE TABLETS.

Prednisolone, as in LENISOLONE TABLETS, 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 medicines

Glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, may increase blood glucose levels. Patients with diabetes mellitus receiving concurrent insulin and/or oral hypoglycaemic medicines may require dosage adjustments of such therapy.

Antiepileptics

Carbamazepine, phenobarbital, phenytoin, and primidone accelerate metabolism of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, and may reduce their effect.

Antifungals

Risk of hypokalaemia may be increased with amphotericin, therefore concomitant use with corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, should be avoided unless corticosteroids are required to control reactions; ketoconazole inhibits metabolism of methylprednisolone and possibly other corticosteroids such as prednisolone, as in LENISOLONE TABLETS.

Antimuscarinics (Anticholinergics)

Prednisolone, as in LENISOLONE TABLETS, has been shown to have antimuscarinic activity. If used in combination with another antimuscarinic medicine could cause impairment to memory and attention in the elderly.

Antithyroids

Prednisolone, as in LENISOLONE TABLETS, clearance is increased by the use of carbimazole and thiamazole.

Antivirals

Plasma concentrations of prednisolone, as in LENISOLONE TABLETS, may be increased with antiviral medicines such as ritonavir and indinavir.

Cardiac glycosides

Increased toxicity if hypokalaemia occurs with corticosteroids, such as prednisolone, as in LENISOLONE TABLETS.

Ciclosporin

Concomitant administration of prednisolone, as in LENISOLONE TABLETS, 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 medicines are administered concomitantly.

Cytotoxics

Increased risk of haematological toxicity with methotrexate.

Hepatic microsomal enzyme inducers

Medicines 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, such as prednisolone, as in LENISOLONE TABLETS, by increasing the rate of metabolism. Lack of expected response may be observed and the dosage of LENISOLONE TABLETS may need to be increased.

Hepatic microsomal enzyme inhibitors

Medicines that inhibit hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4 (e.g. ketoconazole, troleandomycin) may decrease glucocorticoid, such as prednisolone, as in LENISOLONE TABLETS, clearance. Dosages of glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, given in combination with such medicines may need to be decreased to avoid potential adverse effects.

Hormonal contraceptives

Oral contraceptives increased prednisolone, as in LENISOLONE TABLETS, 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, such as prednisolone, as in LENISOLONE TABLETS, are not known, but the particular risk that malignancies in patients undergoing immunosuppression with these or other medicines will spread more rapidly is well-recognised.

Mutual inhibition of metabolism may occur between ciclosporin and prednisolone, as in LENISOLONE TABLETS, and may increase the plasma concentration of either medicine.

Liquorice

Glycyrrhizin can delay the clearance of prednisolone, as in LENISOLONE TABLETS.

Mifepristone

Effect of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, may be reduced for 3 to 4 days after mifepristone.

Non-steroidal anti-inflammatory drugs

Concomitant administration of ulcerogenic medicines such as indomethacin during corticosteroid therapy, such as prednisolone, as in LENISOLONE TABLETS, may increase the risk of GI ulceration. Aspirin should be used cautiously in conjunction with glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, in patients with hypoprothrombinaemia. Although concomitant therapy with salicylate and corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, 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, such as prednisolone, as in LENISOLONE TABLETS, are administered concomitantly. The renal clearance of salicylates is increased by corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, and steroid withdrawal may result in

salicylate intoxication. Salicylates and corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, should be used concurrently with caution. Patients receiving both medicines should be observed closely for adverse effects of either medicine.

Oestrogens

Oestrogens may potentiate the effects of glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, 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, as in LENISOLONE TABLETS, and other corticosteroids by reduction in clearance of prednisolone through the inhibition of P450 isoenzyme CYP3A4.

Other

The desired effects of hypoglycaemic medicines (including insulin), antihypertensives and diuretics are antagonised by corticosteroids, such as prednisolone, as in LENISOLONE TABLETS; and the hypokalaemic effect of acetazolamide, loop diuretics, thiazide diuretics, carbenoxolone and theophylline are enhanced.

Concurrent administration of prednisolone and the potassium depleting diuretics may cause excessive potassium loss.

Somatropin

Growth promoting effect may be inhibited.

Sympathomimetics

Increased risk of hypokalaemia if high doses of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, are given with high doses of bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline.

4.6. Fertility, pregnancy and lactation

The safety of LENISOLONE TABLETS in pregnancy and lactation has not been established.

Pregnancy

The ability of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, to cross the placenta varies between individual medicines, however, 88 % of prednisolone, as in LENISOLONE TABLETS, is inactivated as it crosses the placenta. Administration of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, 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, such as prednisolone, as in LENISOLONE TABLETS, result in an increased incidence of congenital abnormalities, such as cleft palate/lip. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, may increase the risk of intra-uterine growth

retardation. The use of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, during pregnancy may also result in stillbirth. 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, as in LENISOLONE TABLETS, during pregnancy.

Breastfeeding

Corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, are excreted in small amounts in breast milk. Corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants.
The concentration of the steroid, such as prednisolone, as in LENISOLONE TABLETS, 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 > 40 mg/day of prednisolone, as in LENISOLONE TABLETS, is prescribed, the infant should be monitored for adrenal suppression.

Fertility

No data is available on the safety of LENISOLONE TABLETS with regards to fertility.

4.7. Effects on ability to drive and use machines

LENISOLONE TABLETS has a minor influence on the ability to drive or operate machinery.

Since adverse reactions such as dizziness and visual disturbances have been reported in patients taking LENISOLONE TABLETS, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that LENISOLONE TABLETS does not adversely affect their ability to do so (see section 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

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 adults, the frequency of severe reactions has been estimated to be 5 to 6 %. Psychological effects have been reported on withdrawal of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS; the frequency of which, is unknown.

The incidence of predictable undesirable effects, including hypothalamic-pituitary adrenal suppression correlates with the relative potency of the medicine, dosage, timing of administration and the duration of treatment (see section 4.4).

The incidence of side effects rises steeply if dosage increases much above 7,5 mg daily. Short courses at high dosage for emergencies appear to cause less side effects than prolonged courses with lower doses.

b) Tabulated list of adverse reactions

System organ class	Frequent	Less frequent	Frequency unknown (cannot be estimated from the available data)
Infections and infestation			Sepsis, tuberculosis[2.], fungal infections, increased susceptibility to, and severity of infections[1], opportunistic infections*, viral infections, masked feeling of well-being*, oesophageal candidiasis,
Blood and the lymphatic system disorders			Reduction in the number of circulating lymphocytes, leucocytosis.
Immune system disorders			Hypersensitivity including anaphylaxis.
Endocrine disorders			Impaired carbohydrate tolerance with the insulin requirements of diabetic patients increased, manifestation of latent diabetes mellitus, hyperactivity of the adrenal cortex[10] Cushingoid facies, suppression of the hypothalamo-pituitary adrenal axis[3].
Metabolism and nutrition disorders		Calciphylaxis[5].	Sodium and water retention (oedema), electrolyte imbalance, negative nitrogen and calcium balance, hypokalaemic alkalosis, potassium loss, glucose intolerance, protein catabolism, increase in high and low density lipoprotein cholesterol concentration in the blood, weight gain obesity, hyperglycaemia, dyslipidaemia, increased appetite[4],
Psychiatric disorders	Irritability, depressed and labile mood, suicidal thoughts, psychotic reactions, mania, delusions, hallucinations, aggravation of schizophrenia. behavioural		Euphoria, psychological dependence, depression, psychoses.

	disturbances, anxiety, sleep disturbances, cognitive dysfunction including confusion, restlessness, nervousness and amnesia.		
Nervous system disorders			Insomnia, dizziness, headache, raised intracranial pressure with papilloedema (pseudotumor cerebri)[6], aggravation of epilepsy, epidural lipomatosis, vertebrobasilar stroke[7],mental and neurological disturbances.
Eye disorders			Glaucoma, papilloedema, posterior subcapsular cataracts, nuclear cataracts, 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			Vertigo.
Cardiac disorders			Congestive heart failure in susceptible patients, hypertension, increased risk of heart failure, increased risk of cardiovascular disease including myocardial infarction,[9] bradycardia[10.]
Vascular disorders			Thromboembolism.*
Gastrointestinal disorders	Dyspepsia, gastric ulceration.		Nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, diarrhoea, oesophageal ulceration, acute pancreatitis.
Skin and subcutaneous tissue disorders			Hyperhidrosis, buffalo hump, skin thinning. hirsutism, ecchymosis, flushing, increased bruising*, striae, telangiectasia, acne, pruritus, rash, urticaria.
Musculoskeletal and connective tissue disorders			Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, spontaneous fractures, aseptic necrosis of bone, tendon rupture, tendinopathies (particularly of the

			Achilles and patellar tendons), muscular weakness[10],myalgia, growth suppression in infancy, childhood and adolescence.
Renal and urinary disorders			Scleroderma renal crisis*
Pregnancy, puerperium and perinatal conditions			During pregnancy: foetal or neonatal adrenal suppression[10]
Reproductive system and breast disorders			Menstrual irregularity, amenorrhoea.
General disorders and administrative site conditions			Fatigue, malaise, impaired healing.
Investigations			Increased intra-ocular pressure, may suppress reactions to skin tests.

*. see section c).

1. with suppression of clinical symptoms and signs.

2. see section 4.4.

3. particularly in times of stress, as in trauma, surgery or illness.

4. which may result in weight gain.

5. see section 4.4.

6. usually after treatment withdrawal.

7. exacerbation of giant cell arteritis, with clinical signs of evolving stroke has been attributed to prednisolone, as in LENISOLONE TABLETS.

8. see section 4.4.

9. with high dose therapy.

10. following high doses.

c) Description of selected adverse reactions

Withdrawal symptoms

Too rapid a reduction of corticosteroid, such as prednisolone, as in LENISOLONE TABLETS, dosage following prolonged treatment can lead to acute adrenal

insufficiency, hypotension and death (see section 4.4). A steroid 'withdrawal syndrome' seemingly unrelated to adrenocortical insufficiency may also occur following abrupt discontinuance of glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS. 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, such as prednisolone, as in LENISOLONE TABLETS.

Infections and infestations

Increased susceptibility to all kinds of infection, including sepsis, tuberculosis, fungal infections and viral infections has been reported in patients on prednisolone therapy.

Infections may be masked due to marked anti-inflammatory properties with analgesic and antipyretic effects and may produce a feeling of well-being.

The effect on tissue repair is evident by delayed wound healing and increased likelihood of infection.

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 %).

Vascular disorders

Increase in blood coagulability may lead to thromboembolic complications.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/+27 (0)11 239-6200

4.9. Overdose

Symptoms

See section 4.8.

Reports of acute toxicity and/or death following overdosage of glucocorticoids, such as prednisolone, as in LENISOLONE TABLETS, are rare. High systemic doses of corticosteroids, such as prednisolone, as in LENISOLONE TABLETS, caused by chronic use have been associated with adverse effects such as neuropsychiatric disorders (psychosis, depression, and hallucinations), cardiac dysrhythmias and Cushing's syndrome.

Treatment

Treatment is symptomatic and supportive, and where possible the dosage should be reduced or the medicine slowly withdrawn.

No specific antidote is available. Serum electrolytes should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 21.5.1 Corticosteroids and analogues

Pharmacotherapeutic group: Corticosteroids for systemic use.

ATC code: H02AB06

Mechanism of action

Prednisolone is a synthetic glucocorticoid.

Prednisolone has five times the potency of cortisone acetate but in equivalent doses causes less sodium and fluid retention although more gastric symptoms.

5.2. Pharmacokinetic properties

Absorption

Prednisolone is readily absorbed from the gastrointestinal tract.

Distribution

Prednisolone is extensively bound to plasma proteins. Peak plasma concentrations of prednisolone are obtained 1 or 2 hours after administration by mouth, and it usually has a plasma half-life of 2 to 3 hours.

Biotransformation and elimination

Prednisolone is excreted in the urine as free and conjugated metabolites, together with an appreciable amount of unchanged prednisolone.

Prednisolone crosses the placenta and small amounts are excreted in breast milk (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose (102), talc (purified).

6.2. Incompatibilities

Not applicable.

6.3 Shelf life

Amber PVC container: 24 months

Securitainer: 60 months

6.4. Special precautions for storage

Store at or below 25 ºC in airtight containers.

Protect from light.

6.5. Nature and contents of container

Pack size of 100 and 500 tablets: Packed into white cylindrical polypropylene securitainers together with a package insert. The container is stoppered with a white polyurethane foam insert, capped with a white low density polyethylene cap.

Pack size of 1 000 tablets: Packed into white cylindrical polypropylene securitainers together with a package insert. The container is stoppered with a white polyurethane foam insert, capped with a white low density polyethylene cap.

Or

Packed into white opaque HDPE container with a White opaque HDPE screw closure with IS liner.

Pack size of 5 000 tablets: Packed into amber PVC containers together with a package insert. The container is stoppered with a polyurethane foam insert, capped with a white pilfer proof cap.

Not all packs and pack sizes are necessarily marketed.

6.6. Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. APPLICATION NUMBER

G2968 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION

September 1974

10. DATE OF REVISION OF TEXT

21 November 2023

Die Afrikaanse Professionele Inligting is op versoek beskikbaar.

Mediese Blitslyn: 0800 118 088.

Namibia: NS2 14/21.5.1/0540

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