SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

PANAFCORT 5 mg TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Prednisone	5 mg
Contains sugar: Lactose	50,2 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

White, round, normal, convex tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Severe or acute rheumatic, dermatological and allergic conditions, collagen diseases, musculoskeletal conditions.

4.2 Posology and method of administration

Posology

Take with or after food, 2 to 20 tablets daily in divided doses.

Paediatric population

No data are available.

Method of administration

Oral

4.3 Contraindications

- Known hypersensitivity to prednisone or to any of the excipients listed in section 6.1.
- Peptic ulcer
- Osteoporosis
- Psychosis or severe psychoneuroses
- Presence of acute bacterial infections, herpes zoster, herpes simplex, ulceration of the eye and other viral infections.
- Vaccination against smallpox and other infections.
- Liver disease.

4.4 Special warnings and precautions for use

- Immunisation procedures should not be undertaken in patients taking high doses of corticosteroids, such as prednisone, as in PANAFCORT (see section 4.3).
  Live vaccines should be postponed until at least 3 months after stopping treatment with PANAFCORT.
- Use with caution in the presence of congestive heart failure, diabetes mellitus, infectious diseases, chronic renal failure and uraemia and in elderly persons.
- Large doses may produce symptoms typical of hyperactivity of the adrenal cortex, with moon-face, sometimes with hirsutism, buffalo hump, flushing, increased bruising, striae and acne, sometimes

leading to a fully developed Cushing's syndrome.

- On sudden reduction of dosage during the treatment of rheumatoid arthritis, fatalities have been attributed to lesions of small arteries and arterioles similar to polyarteritis, an increase in blood coagulability
  may lead to thromboembolic complications.
- The administration of prednisone may also cause a reduction in the number of circulating lymphocytes.
- Disturbance of electrolyte balance is manifest with the retention of sodium and water, oedema, hypertension and increased excretion of potassium with the possibility of hypokalaemic alkalosis. In extreme cases, cardiac failure may be induced.
- Excessive metabolic effects lead to mobilisation of calcium and phosphorus with osteoporosis and spontaneous fractures, nitrogen depletion.
- The insulin requirements of diabetic patients are increased.
- Patients concurrently taking diuretics which cause potassium depletion should be watched carefully for signs of hypokalaemia.
- Patients with active or doubtfully quiescent tuberculosis should not be given these hormones except as adjuncts to treatment with tuberculostatic medicines. Patients with quiescent tuberculosis should be observed closely and should receive chemoprophylaxis if corticosteroid therapy is prolonged.
- There is normally an increased secretion of corticosteroids by the adrenals in response to infection or stress caused by anaesthesia, surgery or trauma; patients receiving corticosteroids, such as prednisone, as in PANAFCORT, or who have been given corticosteroids in the previous 3 months may have insufficient adrenal reserve and should be given supplementary corticosteroids.
- Hyperglycaemia with accentuation or precipitation of the diabetic state have been reported. The insulin requirements of diabetic patients are increased. Increased appetite is often reported.
- Increased susceptibility to all kinds of infection has been reported, including sepsis, fungous infections and viral infections, e.g., *Candida* infection of the mouth especially if given concomitantly with antibiotics.
- Infections may be masked since steroids, such as prednisone, as in PANAFCORT, have marked anti-inflammatory properties with analgesic and antipyretic effects and may produce a feeling of well-being.
- Caution must be observed in ulcerative colitis if a possibility exists of intestinal perforation and peritonitis.
- Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids, such as prednisone, as in PANAFCORT. PANAFCORT should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.
- Hepatic disease: In patients with acute and active hepatitis, protein binding of the glucocorticoids, such as prednisolone (active form of prednisone, as contained in PANAFCORT), will be reduced and peak concentrations increased. Elimination of glucocorticoids such as prednisolone (active form of prednisone, as contained in PANAFCORT), will also be impaired.
  There is an enhanced effect of corticosteroids such as prednisolone (active form of prednisone, as contained in PANAFCORT), in patients with cirrhosis.
- Menopause, post-menopause: Corticosteroid requirements, such as prednisone, as in PANAFCORT, 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, such as prednisone, as in PANAFCORT (see section 4.3).

- Epilepsy, and/or seizure disorders.
- Previous steroid myopathy.
- Myasthenia gravis: Glucocorticoids, such as prednisone, as in PANAFCORT, should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy.
- Thromboembolic disorders: Cortisone, such as prednisone, as in PANAFCORT, has been reported to increase blood coagulability and to precipitate intravascular thrombosis, thromboembolism, and thrombophlebitis. Corticosteroids, such as prednisone, as in PANAFCORT, should be used with caution in patients with thromboembolic disorders.
- Risk of bradycardia: Bradycardia is rare but serious adverse effect of corticosteroids, such as prednisone, as in PANAFCORT, that may be both symptomatic and asymptomatic. It is most likely to occur with high doses of corticosteroids, such as prednisone, as in PANAFCORT, however, bradycardia can occur even with standard doses of oral corticosteroids, such as prednisone, as in PANAFCORT, 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.
- Duchenne muscular dystrophy: Transient rhabdomyolysis and myoglobinuria may occur following strenuous physical activity. It is not known whether this is due to prednisone, as in PANAFCORT, 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.
- Psychiatric adverse reactions: Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids, such as prednisone, as in PANAFCORT (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 prednisone, as in PANAFCORT, although such reactions have been reported infrequently.

  Particular care is required when considering the use of systemic corticosteroids, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT (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 prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT.
  Pharmacologic doses of corticosteroids, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, have been stopped following prolonged therapy they may need to be temporarily reintroduced.
- 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, such as prednisone, as in PANAFCORT, are used.
  The immunosuppressive effects of glucocorticoids, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, should not be stopped and the dose may need to be increased.
- Measles: Patients taking corticosteroids, such as prednisone, as in PANAFCORT, should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs.
  Ocular effects: Prolonged use of corticosteroids, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT.
  Corticosteroids, such as prednisone, as in PANAFCORT, is contraindicated in patients with ocular

herpes simplex because of possible perforation (see section 4.3).
PANAFCORT should also be used with great caution in the presence of glaucoma.
Systemic glucocorticoid treatment, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, can produce or aggravate Cushing's syndrome, glucocorticoids, such as prednisone, as in PANAFCORT, should be avoided in patients with Cushing's disease.
  There is an enhanced effect of corticosteroids, such as prednisone, as in PANAFCORT, in patients with hypothyroidism.
  Psychic derangements may appear when corticosteroids, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, 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 (active form of prednisone, as contained in PANAFCORT). 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 prednisone, as in PANAFCORT, 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.
  PANAFCORT should be used with great caution in elderly patients.
- Tumour lysis syndrome: In post marketing experience, tumour lysis syndrome (TLS) has been reported in patients with malignancies, including haematological malignancies and solid tumours, following the use of systemic corticosteroids alone, including PANAFCORT, or in combination with other chemotherapeutic medicines. Patients at high risk of TLS, such as patients with tumours that have a high proliferative rate, high tumour burden and high sensitivity to cytotoxic medicines, should be monitored closely and appropriate precautions should be taken.

Paediatric population
Corticosteroids, such as prednisone, as in PANAFCORT, 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
PANAFCORT contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
PANAFCORT contains less than 1 mmol sodium (23 mg) per tablet, that is to say, it is essentially 'sodium-free'.

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 (active form of prednisone, as contained in PANAFCORT), 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 (active form of prednisone, as contained in PANAFCORT), and thus may reduce their effect. Erythromycin inhibits metabolism of methylprednisolone and possibly other corticosteroids such as prednisone, as in as in PANAFCORT.
Prednisolone (active form of prednisone, as contained in PANAFCORT), can lower plasma levels of isoniazid. Where a reduced response during concurrent use is noted, dosage adjustment of isoniazid may be necessary.

Anticoagulants
The efficacy of coumarin anticoagulants and warfarin may be enhanced by concurrent corticosteroid therapy, such as prednisone, as in as in PANAFCORT, and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Antidiabetic medicines
Corticosteroids, such as prednisone, as in PANAFCORT, increases the requirements for antidiabetic.

Antiepileptics
Concurrent use of phenytoin, carbamazepine, phenobarbital, or primidone may lead to an increased metabolism and reduced effect of corticosteroids, such as prednisolone (active form of prednisone, as contained in PANAFCORT).

Antifungals
The risk of hypokalaemia is increased with amphotericin. Corticosteroids, such as prednisone, as in PANAFCORT, should not be given concurrently with amphotericin, unless required to control reactions.
Ketoconazole may inhibit the metabolism of some corticosteroids, such as prednisolone (active form of prednisone, as contained in PANAFCORT), as in PANAFCORT.

Antimuscarinics (Anticholinergics)
Prednisolone (active form of prednisone, as contained in PANAFCORT), 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 (active form of prednisone, as in PANAFCORT), clearance is increased by the use of carbimazole and thiamazole.

Antivirals
Plasma levels of corticosteroids such as prednisolone (active form of prednisone, as contained in PANAFCORT), may be elevated by antiviral medicines such as ritonavir and indinavir.

Cardiac glycosides
The toxicity of cardiac glycosides is increased if hypokalaemia occurs with corticosteroids, such as prednisone, as in PANAFCORT.

Ciclosporin
Ciclosporin increases plasma concentration of prednisolone (active form of prednisone, as contained in PANAFCORT). The need for appropriate dosage adjustment should be considered when these medicines are administered concomitantly.

Cytotoxics
Concurrent use with methotrexate may increase the risk of haematological toxicity.
Hepatic microsomal enzyme inducers
Concurrent use of phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminoglutethimide may lead to an increased metabolism and reduced effect of corticosteroids, such as prednisone, as in PANAFCORT.

Hepatic microsomal enzyme inhibitors
Medicines that inhibit hepatic enzyme cytochrome P-450 (CYP) isoenzyme 3A4 (e.g. ketoconazole) may decrease glucocorticoid, such as prednisolone (active form of prednisone, as contained in PANAFCORT), clearance. Dosages of PANAFCORT, given in combination with such medicines may need to be decreased to avoid potential adverse effects.

Hormonal contraceptives
Oral contraceptives increased prednisolone (active form of prednisone, as contained in PANAFCORT), 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 prednisone, as in PANAFCORT, 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 4.4).
Mutual inhibition of metabolism may occur between ciclosporin and prednisolone (active form of prednisone, as contained in PANAFCORT), and may increase the plasma concentration of either medicine.

Liquorice
Glycyrrhizin can delay the clearance of prednisolone (active form of prednisone, as contained in PANAFCORT).

Mifepristone
Mifepristone may reduce the effect of corticosteroids, such as prednisone, as in PANAFCORT, for 3 to 4 days.

Non-steroidal anti-inflammatory drugs
Concomitant use of aspirin and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) with corticosteroids,

such as prednisone as in PANAFCORT, may cause an increased incidence of gastrointestinal bleeding and ulceration. Aspirin should be used cautiously in conjunction with glucocorticoids, such as prednisone, as in PANAFCORT, in patients with hypoprothrombinaemia. Although concomitant therapy with salicylate and corticosteroids, such as prednisone, as in PANAFCORT), 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 prednisone, as in PANAFCORT, are administered concomitantly. The renal clearance of salicylates is increased by corticosteroids, such as prednisone, as in PANAFCORT, and steroid withdrawal may result in salicylate intoxication. Salicylates and corticosteroids, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT, 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 (active form of prednisone, as contained in PANAFCORT), and other corticosteroids by reduction in clearance of prednisolone through the inhibition of P450 isoenzyme CYP3A4.

Somatropin
Growth promoting effect may be inhibited.
Sympathomimetics
Increased risk of hypokalaemia if high doses of corticosteroids, such as
prednisone, as in PANAFCORT, are given with high doses of bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline.

Other
The desired effects of hypoglycaemic medicines (including insulin),
antihypertensives and diuretics are antagonised by corticosteroids, such as
prednisone, as in PANAFCORT; and the hypokalaemic effect of
acetazolamide, loop diuretics, thiazide diuretics, carbenoxolone and theophylline are enhanced.
Patients concurrently taking diuretics which cause potassium depletion should be watched carefully for signs of hypokalaemia.

4.6 Fertility, pregnancy and lactation
The safety of PANAFCORT in pregnancy and lactation has not been
established.

Pregnancy
Babies born of mothers who received large doses corticosteroids, such as prednisone, as in PANAFCORT, during pregnancy should be watched carefully for signs of hypoadrenalism.

Animal studies have shown that corticosteroids such as prednisone, as in PANAFCORT, when administered to pregnant animals at high doses, may cause foetal malformations.
There is no evidence that corticosteroids cause an increased incidence of congenital anomalies when

given to pregnant women. However, when administered for long periods or repeatedly during pregnancy, corticosteroids such as prednisone, as in PANAFCORT, may increase the risk of intra-uterine growth retardation. The use of corticosteroids, such as prednisone, as in PANAFCORT, during pregnancy may also result in stillbirth.

Cataracts have been observed in infants born to mothers treated with long-term prednisone, as in PANAFCORT, during pregnancy.

Breastfeeding
Corticosteroids, such as prednisone, as in PANAFCORT, pass into breast milk and mothers receiving corticosteroids should be advised not to breastfeed.

Corticosteroids, such as prednisone, as in PANAFCORT, distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants.

Fertility
Corticosteroids, such as prednisone, as in PANAFCORT, may cause irregular menstruation or amenorrhoea.

4.7 Effects on ability to drive and use machines
The effect on the ability to drive or use machinery has not been evaluated.

Undesirable effects, such as dizziness, vertigo, visual disturbances, and fatigue may occur during treatment with PANAFCORT. If affected, patients should not drive or operate machinery.

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 both adults and children. 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 prednisone as in PANAFCORT; however, the frequency 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. 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 not known
Infections and infestations			Septicaemia, tuberculosis, fungal infections, viral infections,

			increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, recurrence of dormant tuberculosis, may mask the signs and symptoms of infection (see section 4.4), oesophageal candidiasis.
Blood and lymphatic system disorders			Increase in blood coagulability leading to thromboembolic complications, decreased circulating lymphocytes, leucocytosis.
Immune system disorders			Hypersensitivity including anaphylaxis.
Endocrine disorders			Adrenal cortex hyperactivity following high doses, impaired carbohydrate tolerance with the Insulin requirements of diabetic patients increased, manifestation of latent diabetes mellitus, Cushingoid facies, suppression of the hypothalamo-pituitary adrenal axis (particularly in times of stress, as in trauma, surgery or illness).
Metabolism and nutrition disorders			Disturbance of electrolyte balance, sodium and water retention, oedema, increased excretion of potassium with the possibility of hypokalaemic alkalosis, mobilisation of calcium and phosphorus with osteoporosis and spontaneous fractures, nitrogen depletion, hyperglycaemia with accentuation or precipitation of the diabetic state, increased insulin requirements of diabetic patients, glucose intolerance, protein catabolism, increase in high- and low-density lipoprotein cholesterol concentration in the blood, weight gain obesity, hyperglycaemia, dyslipidaemia, increased appetite (see section 4.4).
Psychiatric disorders	Irritability, depressed and labile mood, suicidal thoughts,		Euphoria, psychological dependence, depression, psychoses.

	psychotic reactions, mania, delusions, hallucinations, aggravation of schizophrenia. behavioural 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, usually after treatment withdrawal.), aggravation of epilepsy, epidural lipomatosis, vertebrobasilar stroke 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 (see section 4.4)
Ear and labyrinth disorders			Vertigo.
Cardiac disorders			Increased risk of cardiovascular disease including bradycardia (following high doses), myocardial infarction (with high dose therapy), cardiac failure may be induced (see section 4.4).
Vascular disorders			Hypertension, intracranial hypertension, thromboembolic complications.
Gastrointestinal disorders			Peptic, ulceration with haemorrhage and perforation, nausea, 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, 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 (following high doses), 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 (following high doses).
Reproductive system and breast disorders			Amenorrhoea, menstrual irregularity.
General disorders and administrative site conditions			An effect on tissue repair (delayed wound healing, increased liability to infection), fatigue, malaise.
Investigations			Increased intra-ocular pressure, may suppress reactions to skin tests.

c) Description of selected adverse reactions

Withdrawal Symptoms

PANAFCORT should be gradually discontinued after prolonged therapy as rapid withdrawal may cause acute adrenal insufficiency. Too rapid a reduction of corticosteroid, such as prednisone, as in PANAFCORT, 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 prednisone, as in PANAFCORT. 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 prednisone, as in PANAFCORT.

Infections and infestations
Increased susceptibility to all kinds of infection, including sepsis, tuberculosis, fungal infections and viral infections has been reported in patients on prednisone 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 sub-populations, the occurrence of scleroderma renal crisis is variable. 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 %) (see section 4.4).

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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
Reporting can also be done directly to Adcock Ingram Limited at Adcock.aereports@adcock.com.

4.9 Overdose
Symptoms
Reports of acute toxicity and/or death following overdosage of glucocorticoids, such as prednisone, as in PANAFCORT, are infrequent.
See section 4.8 for possible signs and symptoms of overdose.
High systemic doses of corticosteroids, such as prednisone, as in PANAFCORT, 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
No specific antidote is available. Treatment is supportive and symptomatic. Serum electrolytes should be monitored.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacological Classification: A 21.5.1 Corticosteroids and analogues.
Pharmacotherapeutic group: Corticosteroids for systemic use.
ATC code: H02AB06.

Prednisone is a synthetic glucocorticoid. It has anti-inflammatory actions.

Prednisone has properties qualitatively similar to those of cortisone acetate but causes less sodium and fluid retention and is therefore preferred in the treatment of such conditions as asthma, psoriasis, rheumatoid arthritis, thrombocytopenia and ulcerative colitis. Prednisone is not used for adrenal-deficiency states. It is useful in the treatment of the nephrotic syndrome.

Prednisone is inactive until converted to prednisolone in the liver.

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

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 prednisolone and may thereby increase adverse effects.

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

Maize starch
Lactose
Sodium starch glycollate
Sodium lauryl sulphate
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years: Securitainers of 1000’s
2 years: Securitainers of 100, 500’s and 5000’s in a white HDPE bucket

6.4 Special precautions for storage

Store in airtight container at or below 25 °C and protect from light.

6.5 Nature and contents of container

1000's packed into white polypropylene securitainers with a white LDPE snap-on cap or round amber glass bottle with a polypropylene screw-cap.
5000's packed into 1 L white HDPE bucket with handles, with HDPE closures.
100's and 500's packed into polypropylene securitainers with LDPE closures.
Not all pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road
Erand Gardens
Midrand, 1685
Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER(S)

G3054 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

December 1974

10. DATE OF REVISION OF THE TEXT

08 November 2024

Namibia (NS2) : 14/21.5.1/0405
Botswana (S2): B9323895
Zimbabwe: [PP] 2004/17.1/4274