## 1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

**SCHEDULING STATUS**

**S4**

## 1. NAME OF THE MEDICINE

**FLORINEF 0,1 mg tablets**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of FLORINEF contains 0,1 mg fludrocortisone acetate.

Preservative: Sodium benzoate 0,01 % *m/m*

Contains sugar: Lactose anhydrous 58,92 mg, lactose monohydrate 0,7 mg

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Tablets.

Round, uniform, biconvex, white tablet, scored on one side and engraved on the other side with “FT01”.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

FLORINEF is indicated for:

- Partial replacement therapy for primary adrenocortical insufficiency in Addison’s disease.
- Treatment of salt-losing adrenogenital syndrome.

## 4.2. Posology and method of administration

*Posology*

Dosage depends on the severity of the disease and the response of the patient. The lowest possible dose should be used to control the condition being treated and a reduction in dosage should be made (gradually) when possible.

*Adrenocorticoid insufficiency (chronic)*

In primary adrenal insufficiency, such as Addison's disease, the combination of FLORINEF for its mineralocorticoid effect, with a glucocorticoid such as hydrocortisone or cortisone provides substitution therapy approximating normal adrenal activity.

The usual oral dose for adults, adolescents, and elderly patients is one tablet (0,1 mg) of FLORINEF. The daily range is one tablet (0,1 mg) three times a week to two tablets (0,2 mg) daily.

If treatment-associated hypertension develops, the dose should be reduced to 0,05 mg daily.

FLORINEF is administered preferably in conjunction with cortisone (10 mg to 37,5 mg daily in divided doses) or hydrocortisone (10 mg to 30 mg daily in divided doses).

*Salt-losing adrenogenital syndrome*

The recommended oral dosage for treating salt-losing adrenogenital syndrome is one tablet (0,1 mg) to two tablets (0,2 mg) of FLORINEF daily.

*Paediatric and adolescents*

Salt-losing adrenogenital syndrome: One-half tablet (0,05 mg) to one tablet (0,1 mg) daily.

The need may decrease with age and therefore the dose should be titrated to the clinical requirements of the child.

*Method of administration*

FLORINEF is given orally.

## 4.3. Contraindications

FLORINEF is contraindicated in:

- Patients with hypersensitivity to the fludrocortisone acetate or to any of the excipients in FLORINEF (see section 2 and section 6.1).
- Systemic infections unless specific anti-infective therapy is employed (see section 4.4).
- The treatment of conditions other than those indicated (due to its marked effect on sodium retention).
- Tuberculosis, acute psychosis, ocular herpes simplex, active peptic ulcer, acute glomerulonephritis, fungal diseases, vaccinia, and varicella.
- Patients with uncontrolled congestive heart failure.
- Use of live vaccines (see 4.4).
- Pregnancy and lactation (see 4.4).

## 4.4. Special warnings and precautions for use

*Hypersensitivity reactions*

Instances of anaphylactoid reactions have occurred in patients receiving corticosteroids, including FLORINEF, especially when a patient has a history of medicine allergies.

*Dosage and salt intake*

Since FLORINEF is a potent mineralocorticoid both the dosage and salt intake should be

carefully monitored to avoid the development of hypertension, oedema or weight gain. Periodic checking of serum electrolyte levels is advisable during prolonged therapy.

Although glucocorticoid side effects may occur with FLORINEF, these can be reduced by reducing the dosage.

Undesirable effects may be minimised using the lowest effective dose for the minimum period. Frequent patient review is required to titrate the dose appropriately against disease activity (see section 4.2).

*Prolonged therapy*

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Adverse reactions to FLORINEF may be produced by too rapid withdrawal or by continued use of large doses. Withdrawal of FLORINEF after prolonged therapy must, therefore, always be gradual to avoid acute adrenal insufficiency and should be tapered off over weeks or months according to the dose and duration of treatment. To avoid adrenal insufficiency, patients on long-term systemic therapy with FLORINEF, may require supportive corticosteroid therapy in times of stress (such as trauma, surgery or severe illness) both during the treatment period and up to a year afterwards. If corticosteroids, including FLORINEF, have been stopped following prolonged therapy, they may need to be reintroduced temporarily.

An adequate protein intake is advised for patients on long-term use to counteract any tendency to weight-loss or muscle wasting/weakness associated with negative nitrogen balance.

*Anti-inflammatory/immunosuppressive effects*

The anti-inflammatory effect of corticosteroids, including FLORINEF, may mask symptoms of infection and permit the spread of an invading organism. If an infection occurs during FLORINEF therapy, it should be promptly controlled by suitable antimicrobial therapy (see section 4.3).

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. There may also be decreased resistance and inability to localise infection when FLORINEF is used.

Chickenpox, shingles and measles are of particular concern since these illnesses may be fatal in immunosuppressed patients. Patients should be advised to avoid exposure to these diseases, and to seek medical advice without delay if exposure occurs. Even infections such as herpes zoster, or threadworm infestations, can have a more serious or even fatal course in non-immune children or adults on FLORINEF.

*Vaccinations*

Patients should not be vaccinated or immunised while on FLORINEF therapy, especially on high doses, because of a lack of antibody response predisposing to medical complications, particularly neurological ones. Live vaccines should not be administered (see section 4.3).

*Chickenpox*

Unless they have had chickenpox, patients receiving oral corticosteroids, including FLORINEF, for purposes other than replacement should be regarded as being at risk of severe chickenpox. Manifestations of fulminant illness include pneumonia, hepatitis and

disseminated intravascular coagulation; rash is not necessarily a prominent feature. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids, including FLORINEF or who have used them within the previous 3 months; this should preferably be given within 3 days of exposure, and not later than 10 days after exposure to chickenpox. Confirmed chickenpox warrants specialist care and urgent treatment. Corticosteroids, including FLORINEF, should not be stopped, and the dose may need to be increased.

*Measles*

Prophylaxis with normal immunoglobulin may be needed.

*Tuberculosis*

Latent or healed tuberculosis, in the presence of local or systemic viral infection, systemic fungal infections or in active infections not controlled by antibiotics require frequent patient monitoring.

The use of FLORINEF tablets in patients with active tuberculosis should be restricted to cases of fulminating or disseminated tuberculosis in which FLORINEF is used for the management of the disease in conjunction with an appropriate antituberculous regimen. The emergence of active tuberculosis can, however, be prevented by the prophylactic use of anti-tuberculosis therapy. Chemoprophylaxis should be used in patients with latent tuberculosis or tuberculin reactivity who are taking FLORINEF.
Special care should be taken with patients with a previous history of, or X-ray changes characteristic of, tuberculosis.

*Pheochromocytoma Crisis*

Pheochromocytoma crisis, which can be fatal, has been reported after administration of

systemic corticosteroids to patients with suspected or identified pheochromocytoma. Corticosteroids should only be administered to these patients after an appropriate risk/benefit evaluation.

*Special patient populations*

Care/caution is required when considering use of FLORINEF in patients with the following conditions and frequent patient monitoring is necessary:

- Nonspecific ulcerative colitis (if there is a probability of perforation, abscess, or other pyogenic infection);
- recent intestinal anastomoses;
- diverticulitis;
- thrombophlebitis or thromboembolism;
- existing or previous history of severe affective disorders (especially previous steroid psychosis);
- exanthematous disease (exanthema);
- Cushing's syndrome;
- diabetes mellitus;
- convulsive disorders (epilepsy);
- chronic nephritis, renal insufficiency, acute glomerulonephritis;
- metastatic carcinoma;
- myasthenia gravis;
- in acute psychoses;
- hypertension;
- congestive heart failure (see section 4.3);
- glaucoma (or a family history of glaucoma);
- previous steroid myopathy;

- liver failure.

*Menstrual irregularities*

Corticosteroid therapy, including FLORINEF, has caused menstrual irregularities (see section 4.8).

*Peptic ulcer*

Corticosteroid therapy, including FLORINEF, has caused hyperacidity or peptic ulcer. Patients with an active peptic ulcer should not receive FLORINEF (see section 4.3) and those with a history of peptic ulcer require frequent monitoring.

*Hypothyroidism*

There is an enhanced corticosteroid effect in patients with hypothyroidism or decreased in hyperthyroid patients.

*Cirrhosis*

Corticosteroid, including FLORINEF, effects may be enhanced in patients with cirrhosis.

*Diabetes mellitus*

Diabetes may be aggravated, necessitating a higher insulin dosage. Latent diabetes mellitus may be precipitated (see section 4.8).

*Hypoprothrombinaemia*

Aspirin should be used cautiously in conjunction with corticosteroids, including FLORINEF, in patients with hypoprothrombinaemia.

*Osteoporosis*

FLORINEF increases calcium excretion, which may predispose to osteoporosis or aggravate pre-existing osteoporosis; post-menopausal females are particularly at risk (see section 4.8).

*Visual disturbance*

Visual disturbance may be reported with systemic corticosteroid, including FLORINEF, use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic corticosteroids, including FLORINEF.

Prolonged use of FLORINEF may produce posterior subcapsular cataracts or glaucoma, with possible damage to the optic nerve. Prolonged use may also enhance the likelihood of secondary ocular infections.

FLORINEF should not be used in patients with ocular herpes simplex because of possible corneal perforation.

*Psychiatric adverse reactions*

Potentially severe psychiatric adverse reactions may occur with systemic steroids, such as FLORINEF (see section 4.8). Symptoms typically emerge within a few days or weeks of starting treatment with a systemic steroid such as FLORINEF. Risks may be higher with high doses/systemic exposure 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/caregivers should be encouraged to seek medical advice if worrying psychological

symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/caregivers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

Care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first-degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis. The use of antidepressant medicine does not relieve and may exacerbate andrenocorticoid-induced mental disturbances.

*Paediatric population*

Because corticosteroids, including FLORINEF, can suppress growth, the growth and development of infants, children and adolescents on prolonged corticosteroid therapy, including FLORINEF should be carefully monitored. Corticosteroids, such as FLORINEF, cause dose-related growth retardation in infancy, childhood and adolescence which may be irreversible.

Caution should be used in the event of chicken pox, measles or other communicable diseases. Children should not be vaccinated while on therapy with FLORINEF. Corticosteroids, including FLORINEF may also affect endogenous steroid production.

*Elderly population*

The common adverse effects of systemic corticosteroids, including FLORINEF, may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

The adverse effects of systemic corticosteroids, including FLORINEF, such as osteoporosis or hypertension, may be associated with more serious consequences in the elderly. Therefore, close clinical supervision is recommended.

*Excipients*

*Lactose warning:*

FLORINEF contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take FLORINEF.

**4.5. Interaction with other medicines and other forms of interaction**

When administered concurrently, the following medicines may interact with adrenal corticosteroid, including FLORINEF:

*Amphotericin B (injection) or potassium-depleting medicines (benzothiadiazines and related medicines, ethacrynic acid and furosemide):*

Enhanced hypokalaemia. Potassium levels should be checked at frequent intervals and potassium supplements used if necessary (see section 4.4).

*Anticholinesterases:*

Effects of the anticholinesterase medicine may be antagonised.

*Oral anticoagulants:*

FLORINEF may potentiate or decrease anticoagulant action. Patients receiving oral anticoagulants and FLORINEF should therefore be closely monitored.

*Antidiabetics (oral medicines and insulin):*

Corticosteroids, including FLORINEF, may increase blood glucose or diminish the antidiabetic effect. Patients should be monitored for symptoms of hyperglycaemia especially when FLORINEF is initiated, discontinued, or changed in dosage.

The dosage of antidiabetic medicine should be adjusted if necessary.

*Antihypertensives, including diuretics:*

Corticosteroids, including FLORINEF, antagonise the effects of antihypertensives and diuretics. The hypokalaemic effect of diuretics, including acetazolamide, is enhanced.

*Antitubercular medicine:*

Isoniazid serum concentrations may be decreased in some patients.

*Ciclosporin:*

Increased activity of both ciclosporin and FLORINEF may occur when the two are used concurrently. Patients should be monitored for evidence of increased toxicity of ciclosporin.

*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.

*Digitalis glycosides:*

Enhanced possibility of dysrhythmias or digitalis toxicity associated with hypokalaemia.

Potassium levels should be monitored, and potassium supplements used if necessary.

*Oestrogens, including oral contraceptives:*

The half-life and concentration of FLORINEF may be increased and clearance decreased. A reduction in FLORINEF dosage may be required when oestrogen therapy is initiated, and an increase required when oestrogen is stopped.

*Hepatic enzyme inducers (e.g., aminoglutethemide, barbiturates, phenytoin, carbamazepine, primidone, rifabutin, rifampicin):*

There may be increased metabolic clearance of FLORINEF. Patients should be observed for possible diminished effect of FLORINEF, and the dosage of FLORINEF should be adjusted accordingly.

*Human growth hormone (e.g. somatrem, somatropin):*

The growth-promoting effect of growth hormones such as somatrem and somatropin may be inhibited.

*Ketoconazole:*

FLORINEF clearance may be decreased, resulting in increased therapeutic effect.

*Nondepolarising muscle relaxants:*

FLORINEF may decrease or enhance the neuromuscular blocking action.

*Nonsteroidal anti-inflammatory drugs (NSAIDs):*

FLORINEF may increase the incidence and/or severity of gastrointestinal bleeding and ulceration associated with NSAIDs. FLORINEF can reduce serum salicylate levels and therefore decrease their effectiveness. Conversely, discontinuing FLORINEF during high-

dose salicylate therapy may result in salicylate toxicity. Aspirin should be used cautiously in conjunction with FLORINEF in patients with hypoprothrombinaemia (see section 4.4).

*Thyroid medicine:*

Metabolic clearance of FLORINEF is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in FLORINEF dosage.

*Vaccines:*

Neurological complications and lack of antibody response may occur when patients taking FLORINEF are vaccinated (see section 4.3 and 4.4).

*Laboratory test interactions:*

FLORINEF may affect the nitroblue tetrazolium test for bacterial infection, producing false-negative results.

## 4.6. Fertility, pregnancy and lactation

The use of steroid medicines such as FLORINEF is contraindicated during pregnancy due to known teratogenicity (see 4.3)

**Pregnancy**

If a woman requires mineralocorticoid therapy, effective contraception should be used. Should the woman become pregnant, she must be appraised of the potential foetal toxicity from FLORINEF. The physiological changes inherent with pregnancy, may alter the patients dose requirements.

There is a risk of cleft palate and intra-uterine growth retardation. Hypoadrenalism may

occur in the neonate. Patients with pre-eclampsia or fluid retention require close monitoring for aggravation of the mother's pathology.

The use of steroids during pregnancy, particularly the first trimester, calls for extreme caution, and infants whose mothers have been receiving FLORINEF should be examined carefully at birth for signs of hypoadrenalism and other abnormalities.
Maternal treatment should be carefully documented in the infant's medical records to assist in follow up.

**Lactation**

Corticosteroids, including FLORINEF, are found in breast milk.

Mothers who are receiving FLORINEF, should not breastfeed their infants.

**Fertility**

There are insufficient fertility data available to indicate whether fludrocortisone acetate, as in FLORINEF, has any effect on fertility.

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

FLORINEF may influence the ability to drive and use machines since side effects such as loss of consciousness and blurred vision have been reported in patients receiving FLORINEF (see section 4.8).

## 4.8. Undesirable effects

*a) Tabulated list if adverse reactions*

| **System organ class** | ***Frequent*** | ***Less frequent*** | ***Frequency unknown*** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| **Infections and infestations** | | | Increased susceptibility and severity of infections with suppression of clinical symptoms and signs (masking of infections), opportunistic infections, recurrence of dormant tuberculosis, candidiasis, exacerbation of ophthalmic viral or fungal diseases |
| **Blood and the lymphatic system disorders** | | | Leucocytosis |
| **Immune system disorders** | | | Anaphylactic reactions |
| **Endocrine disorders** | | | Cushingoid state (changes such as facial rounding, buffalo hump or other signs of fat deposition), suppression of growth in childhood and adolescence, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress (e.g. trauma, surgery or illness)), |
| **Metabolism and nutrition disorders** | Hypokalaemia | Hypokalaemic alkalosis, decreased appetite (anorexia) | Sodium retention, fluid retention, activation of latent diabetes mellitus or aggravation of existing diabetes and increased requirements for |

| | | | |
|---|---|---|---|
| | | | insulin or oral hypoglycaemic medicines in diabetes, weight gain, increased appetite |
| **Psychiatric disorders** | Affective disorders (such as irritable, euphoric, depressed (sometimes severe), labile moods (mood swings), suicidal thoughts), psychotic symptoms (including mania, delusions, hallucinations, and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances | Delusional perception, illusion | Psychological dependence, insomnia, aggravation of pre-existing psychiatric conditions, severe mental disturbances, changes in personality |
| **Nervous system disorders** | Headache, cognitive dysfunction (including confusion and amnesia) | Seizure, epilepsy, syncope, loss of consciousness, dysgeusia (taste perversion) | Convulsions, increased intracranial pressure with papilloedema (pseudo-tumour cerebri), neuritis, paraesthesia |
| **Eye disorders** | | | Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos, papilloedema, corneal or scleral thinning, blurred vision |
| **Ear and labyrinth disorders** | | | Vertigo |

| | | | |
|---|---|---|---|
| **Cardiac disorders** | Congestive cardiac failure in susceptible patients | Cardiomegaly (cardiac enlargement) | Cardiac dysrhythmias (due to potassium deficiency) |
| **Vascular disorders** | Hypertension | | Necrotising angiitis, thrombophlebitis, thromboembolism |
| **Gastrointestinal disorders** | | Diarrhoea | Dyspepsia, activation or aggravation of peptic ulcer (possible subsequent perforation and haemorrhage), pancreatitis, abdominal distension, ulcerative oesophagitis, minor gastrointestinal difficulties |
| **Skin and subcutaneous tissue disorders** | | | Angioedema, rash, pruritus, urticaria, thin fragile skin, petechiae, ecchymoses, facial erythema, increased sweating, bruising or purpura, striae, hirsutism, acneiform eruptions, lupus erythematosus-like lesions, subcutaneous fat atrophy |
| **Musculoskeletal, connective tissue and bone disorders** | Muscular weakness | Muscle atrophy (wasting of skeletal muscle) | Steroid myopathy, loss of muscle mass, osteoporosis, avascular osteonecrosis, vertebral compression |

| | | | |
|---|---|---|---|
| | | | fractures, delayed healing of fractures, aseptic necrosis of femoral and humeral heads (hip), pathological fractures of long bones and spontaneous fractures, tendon rupture, myasthenia |
| **Reproductive system and breast disorders** | | | Menstrual irregularities (disturbances), amenorrhoea |
| **General disorders and administrative site conditions** | Oedema, swelling | | Fatigue, impaired wound healing, withdrawal syndrome (symptoms include fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss may occur. Too rapid a reduction in dose following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death) |
| **Investigations** | | Decreased blood potassium | Potassium loss, increased calcium excretion, suppressed reactions to skin tests, negative protein and calcium balance, ECG changes (due to potassium deficiency), decreased |

| | | | |
|---|---|---|---|
| | | | carbohydrate tolerance |

*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

**4.9 Overdose**

**Symptoms**

Development of hypertension, oedema, hypokalaemia, significant increase in weight, and increase in heart size may be signs of excessive dosage of FLORINEF. Muscle weakness due to excessive potassium loss may develop and can be treated with potassium supplements. Monitoring of blood pressure and serum electrolytes can reduce the likelihood of consequences of excessive dosage (see section 4.4).

**Treatment**

Treatment of overdosage should be symptomatic and supportive.

When symptoms are noted, administration of FLORINEF should be discontinued, after

which the symptoms will usually subside within several days; subsequent treatment with FLORINEF, if necessary, should be resumed at a reduced dose.

For large, acute overdoses, treatment includes gastric lavage or emesis and usual supportive measures.

A single large dose should be treated with plenty of water by mouth. Careful monitoring of serum electrolytes is essential, with particular consideration being given to the need for administration of potassium chloride and restriction of dietary sodium intake.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Category and Class: A 21.5.1 Corticosteroids and analogues

Pharmacotherapeutic group: Corticosteroids for systemic use, plain

ATC Code: H02AA02

*Mechanism of action*

Fludrocortisone acetate is a synthetic adrenocortical steroid with potent mineralocorticoid properties and high glucocorticoid activity. It is used for its mineralocorticoid effects.

Corticosteroids, such as fludrocortisone, are thought to act, at least in part, by controlling the rate of synthesis of proteins at the cellular level. The relationship between this activity and the metabolic effects is not yet totally clear.

The physiologic action of fludrocortisone acetate is similar to that of hydrocortisone, but the glucocorticoid effect is 15 times as potent and the mineralocorticoid effect is 125 times greater (particularly on electrolyte balance, and also on carbohydrate metabolism are

considerably heightened and prolonged).

Since fludrocortisone acetate exerts so profound a mineralocorticoid effect, its usefulness is limited to clinical applications which utilise this effect, and it should not be used as an anti-inflammatory medicine for the treatment of such cortisone-responsive diseases as rheumatoid arthritis, certain allergies, and dermatoses.

Small oral doses of fludrocortisone acetate produce marked sodium retention and increased urinary potassium excretion. Fludrocortisone acetate also causes a rise in blood pressure, apparently because of these effects on electrolyte levels. In larger doses, the steroid inhibits endogenous adrenal cortical secretion, thymic activity, and pituitary corticotropin secretion; promotes the deposition of liver glycogen; and, unless protein intake is adequate, induces negative nitrogen balance.

## 5.2. Pharmacokinetic properties

**Absorption**

Sodium reabsorption in the renal distal tubules and in other tissues appears to account for the physiologic action characteristic of mineralocorticoids.

**Distribution**

Fludrocortisone is highly protein bound. Small doses of these medicines result in marked sodium retention and increased urinary excretion of potassium and hydrogen.

**Biotransformation**

Blood pressure is also elevated apparently because of these effects on electrolytes. Larger doses inhibit endogenous adrenal cortical secretion, thymic activity, and pituitary corticotropin excretion; high doses also promote the deposition of liver glycogen, and

unless protein intake is adequate, induce negative nitrogen balance.

**Elimination**

The pharmacokinetic half-life of fludrocortisone is approximately 5,5 hours. Fludrocortisone is eliminated by the kidneys, mostly as inactive metabolites. The pharmacodynamic half-life of fludrocortisone is approximately 18 to 36 hours. The duration of action is 1 to 2 days.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Dibasic calcium phosphate, lactose anhydrous, lactose monohydrate, magnesium stearate, maize starch, sodium benzoate, talc.

### 6.2. Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months

### 6.4 Special precautions for storage

Store in a refrigerator, at 2 °C to 8 °C, in a well-closed container. Excursions to room temperature (25 °C) are permitted for up to 30 days. After temperature excursion, do not return unused tablets to refrigerated storage and dispose of such tablets properly.
Keep in original packaging until required for use.

### 6.5. Nature and contents of container

100 tablets are packed in a brown glass bottle and sealed with a white polypropylene screw cap with tamper evidence and sealing disc, together with cotton or rayon, and a

leaflet.

### 6.6 Special precautions for disposal

No special requirements.

## 7. HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

## 8. REGISTRATION NUMBER

G3134 (Act 101 of 1965)

## 9. DATE OF FIRST AUTHORISATION

Date of registration: Old medicine

## 10. DATE OF REVISION OF TEXT

02 November 2023

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