NEW ZEALAND DATA SHEET

1. PRODUCT NAME

FLUDROCORTISONE MEDSURGE 0.1 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Fludrocortisone acetate tablets contain 0.1 mg of fludrocortisone acetate.

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

White or off-white, oblong tablets, with a score line on one side.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Partial replacement therapy for primary adrenocortical insufficiency in Addison's disease and for the treatment of salt losing adrenogenital syndrome.

4.2 DOSE AND METHOD OF ADMINISTRATION

Addison's Disease

The combination of fludrocortisone acetate tablets with a glucocorticoid such as hydrocortisone or cortisone provides substitution therapy approximating normal adrenal activity with minimal risks of unwanted effects. The usual dose is 0.1 mg of fludrocortisone acetate tablets daily, although dosage ranging from 0.1 mg three times a week to 0.2 mg daily has been employed. In the event transient hypertension develops as a consequence of therapy, the dose should be reduced to 0.05 mg daily. Fludrocortisone acetate tablets is preferably administered in conjunction with cortisone (10 to 37.5 mg daily in divided doses) or hydrocortisone (10 to 30 mg daily in divided doses).

Salt-losing adrenogenital syndrome

The recommended dosage is 0.1 to 0.2 mg of fludrocortisone acetate tablets daily.

4.3 CONTRAINDICATIONS

Patients with systemic fungal infections.

Patients with suspected or known hypersensitivity to fludrocortisone or any on the inactive ingredients.

Patients on high dose fludrocortisone acetate tablets should not be administered live vaccines

as the antibody response will be reduced (see section 4.4 Special warnings and precautions for use).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Because of its marked effect on sodium retention, the use of fludrocortisone acetate tablets in the treatment of conditions other than those indicated herein is not advised.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used. If an infection occurs during fludrocortisone acetate therapy, it should be promptly controlled by suitable antimicrobial therapy. Chicken pox, measles, herpes zoster, or threadworm infestations for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid 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 and topical corticosteroids.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased potassium excretion. These effects are less likely to occur with the synthetic derivatives except when used in large doses. However, since fludrocortisone acetate is a potent mineralocorticoid, both the dosage and salt intake should be carefully monitored in order to avoid the development of hypertension, oedema or weight gain.

Fludrocortisone acetate tablets should not be used in patients with uncontrolled congestive heart failure.

Periodic checking of serum electrolyte levels is advisable during prolonged therapy; dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion, which may predispose to osteoporosis or aggravate preexisting osteoporosis.

Vaccination

Live vaccines are contraindicated in patients taking high doses of Fludrocortisone acetate tablets (see section 4.3 Contraindications). Live vaccines may, however, be administered to patients on maintenance therapy, although there may be a reduced response. Killed or inactivated vaccines do not represent a danger to immunocompromised patients and generally should be administered as for healthy children. However, there may be a reduced response.

The use of fludrocortisone acetate tablets in patients with active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary since reactivation of the disease may occur. During

prolonged corticosteroid therapy these patients should receive chemoprophylaxis.

Adverse reactions to corticosteroids may be produced by too rapid withdrawal or by continued use of large doses.

To avoid drug induced adrenal insufficiency, supportive dosage may be required in times of stress (such as trauma, surgery or severe illness) both during treatment with fludrocortisone acetate and for a year afterwards.

There is an enhanced corticosteroid effect in patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular Herpes simplex because of possible corneal perforation.

The lowest possible dose of corticosteroid should be used to control the condition being treated. A gradual reduction in dosage should be made when possible.

Psychiatric disturbances may appear when corticosteroids are used. These may range from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic tendencies may also be aggravated by corticosteroids.

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

The use of antidepressant drugs does not relieve and may exacerbate adreno-corticosteroid induced mental disturbances.

Corticosteroids should be used with caution in patients with nonspecific ulcerative colitis if there is a probability of impending perforation, abscess, or other pyogenic infection.

Corticosteroids should also be used cautiously in patients with diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, acute glomerulonephritis, vaccinia, varicella, exanthema, Cushing's syndrome, antibiotic resistant infections, diabetes mellitus, congestive heart failure, chronic nephritis, thromboembolic tendencies, thrombophlebitis, convulsive disorders, metastatic carcinoma and myasthenia gravis. Further, corticosteroid therapy has caused menstrual irregularities and hyperacidity or peptic ulcer.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

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

Patients should be monitored regularly for blood pressure and serum electrolyte levels.

Use in the elderly

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

Pediatric use

Safety and effectiveness of fludrocortisone acetate tablets have not been established in

children. Because corticosteroids can suppress growth, the growth and development of infants and children and adolescents on prolonged corticosteroid therapy should be carefully monitored. Caution should be used in the event of chicken pox, measles, or other communicable diseases. Children may be vaccinated while on maintenance therapy with fludrocortisone acetate tablets (see section 4.4 Special warnings and precautions for use). Corticosteroids may also affect endogenous steroid production.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

When administered concurrently, the following drugs may interact with adrenal corticosteroids:

Amphotericin B or potassium-depleting diuretics (benzothiadiazines and related drugs, ethacrynic acid and furosemide) --Enhanced hypokalemia. Potassium levels should be checked at frequent intervals and potassium supplements used if necessary (see section 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Anticholinesterases--Effects of the anticholinesterase agent may be antagonized.

Anticoagulants oral--Corticosteroid may potentiate or decrease anticoagulant action. Patients receiving oral anticoagulants and corticosteroids should therefore be closely monitored.

Antidiabetics (oral agents and insulin) Diminished antidiabetic effect. Patient should be monitored for symptoms of hyperglycemia; dosage of antidiabetic drug should be adjusted if necessary.

Antitubercular drugs--Isoniazed serum concentrations may be decreased in some patients.

Cyclosporin--Increased activity of both cyclosporin and corticosteroids may occur when the two are used concurrently.

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

Digitalis glycosides--Enhanced possibility of arrhythmias or digitalis toxicity associated with hypokalemia. Potassium levels should be monitored, and potassium supplements used if necessary.

Estrogens, including oral contraceptives--Corticosteroid half-life and concentration may be increased and clearance decreased. A reduction in corticosteroid dosage may be required when estrogen therapy is initiated, and an increase required when estrogen is stopped.

Hepatic Enzyme Inducers (eg, barbiturates, phenytoin, carbamazepine, rifampin) --Increased metabolic clearance of fludrocortisone. Patients should be observed for possible diminished effect of steroid, and the dosage of fludrocortisone acetate tablets should be adjusted accordingly.

Human growth hormone (eg, somatrem) --The growth-promoting effect of somatrem may be inhibited.

Ketoconazole--Corticosteroid clearance may be decreased, resulting in increased therapeutic effect.

Nondepolarizing muscle relaxants--Corticosteroids may decrease or enhance the neuromuscular blocking action.

Nonsteroidal anti-inflammatory agents (NSAIDs)--Increased ulcerogenic effect; decreased pharmacologic effect of aspirin. Conversely, salicylate toxicity may occur in patients who discontinue steroids with concurrent high-dose aspirin therapy. Corticosteroids should be used cautiously in conjunction with aspirin in patients with hypoprothrombinemia.

Thyroid drugs--Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in adrenocorticoid dosage.

Vaccines--Neurological complications and lack of antibody response may occur when patients taking corticosteroids are vaccinated (see section 4.4 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Laboratory test interactions--Corticosteroids may effect the nitroblue tetrazolium test for bacterial infection, producing false-negative results.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category C

In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations) and abortion. These findings do not seem to be relevant to humans. Reduced placental and birth weight have been recorded in animals and humans after long-term treatment. Since the possibility of suppression of the adrenal cortex in the newborn infant after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the foetus when prescribing these drugs. The short-term use of corticosteroids antepartum for the prevention of respiratory distress syndrome does not seem to pose a risk to the foetus or the newborn infant.

Infants born of mothers who have received substantial doses of fludrocortisone acetate during pregnancy should be carefully observed for signs of hypoadrenalism. Maternal pulmonary oedema has been reported with tocolysis and fluid overload.

Use in lactation

The use of this drug in nursing mothers requires that the possible benefits of the drug be weighed against the potential hazards to the child.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not applicable.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

In the recommended small dosages, the side effects seen with cortisone and its derivatives are not usually a problem with fludrocortisone. However, the following untoward effects should be kept in mind, particularly when this agent is used over a prolonged period of time or in conjunction with cortisone or a similar glucocorticoid.

Fluid and electrolyte disturbances. Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalaemic alkalosis and hypertension.

Musculoskeletal. Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis or femoral and humeral heads, pathologic fracture of long bones and spontaneous fractures.

Gastrointestinal. Peptic ulcer with possible perforation and haemorrhage, pancreatitis, abdominal distension, hyperacidity, ulcerative oesophagitis , anorexia, taste perversion and diarrhoea.

Dermatological. Impaired and wound healing, thin fragile skin, bruising, petechiae and ecchymoses, facial erythema, increased sweating, subcutaneous fat atrophy, purpura, striae, hyperpigmentation of the skin and nails, hirsutism, and acne-form eruptions; reactions to skin tests may be suppressed.

Neurological. Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache and severe mental disturbances and hallucinations..

Endocrine. Menstrual irregularities, development of the cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress (e.g. trauma, surgery or illness), decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, and increased requirements for insulin or oral hypoglycaemic agents in diabetes.

Ophthalmic. Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos.

Metabolic. Hyperglycaemia, glycosuria and negative nitrogen balance due to protein catabolism.

Other. Other adverse reactions that may occur following the administration of a corticosteroid are necrotising angitis, thrombophlebitis, aggravation or masking of infections, insomnia, syncopal episodes and anaphylactoid reactions.

4.9 OVERDOSE

Chronic

Development of hypertension, edema, hypokalemia, significant increase in weight, and increase in heart size may be signs of excessive dosage of fludrocortisone acetate tablets.

When these are noted, administration of the drug should be discontinued, after which the symptoms will usually subside within several days; subsequent treatment with fludrocortisone acetate tablets, if necessary, should be resumed at a reduced dose. 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 – SPECIAL WARNINGS AND PRECAUTIONS FOR USE).**

Acute
For large, acute overdoses, treat symptomatically and institute usual supportive measures as required.

For information on the management of overdose, contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

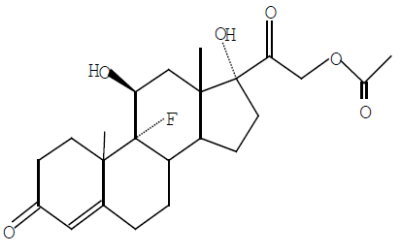
Fludrocortisone acetate is a synthetic adrenocortical steroid possessing very potent mineralocorticoid properties and high glucocorticoid activity. It is used for its mineralocorticoid effects.

5.1 PHARMACODYNAMIC PROPERTIES

The chemical name is 9-Fluoro-11β,17-dihydroxy-3,20-dioxopregn-4-en-21-yl acetate.

It is a white to pale yellow, odourless or almost odourless, crystalline powder. Practically insoluble in water; soluble 1 in 50 in alcohol, 1 in 50 in chloroform; slightly soluble in ether.

Chemical structure



CAS number

514-36-3

Drug class: corticosteroid; glucocorticoid; ATC code: H02AA02

Actions
The physiological action is similar to that of hydrocortisone. However, the effects of fludrocortisone acetate, particularly on electrolyte balance, but also on carbohydrate metabolism, are considerably heightened and prolonged. In small oral doses, it produces marked sodium retention and increased urinary potassium excretion. It also causes a rise in blood pressure, apparently because of these effects on electrolyte levels.

5.2 PHARMACOKINETIC PROPERTIES

In larger doses, fludrocortisone acetate inhibits endogenous adrenal cortical secretion, thymic activity, and pituitary corticotropin excretion; promotes the deposition of liver glycogen; and, unless protein intake is adequate, induced negative nitrogen balance. The approximate half-life of fludrocortisone is 18-36 hours. It is highly protein bound and is eliminated by the kidney's, mostly as inactive metabolites. Duration of action is 1 to 2 days.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

microcrystalline cellulose,
mannitol,
hypromellose,
croscarmellose sodium,
colloidal anhydrous silica,
magnesium stearate.

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF LIFE

36 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

The tablets are packed in PVDC/PVDC/Alu blister. Pack sizes of 30 & 100 tablets.

(Note: Not all pack sizes are marketed.)

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

7 MEDICINE SCHEDULE

Prescription medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

15 December 2022

10 DATE OF REVISION

Not applicable

SUMMARY TABLE OF CHANGES

New datasheet