

 **3 July 2025**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**Fludrocortisonacetat "Galen", tablets**

**0. D.SP.NO.**

33726

**1. NAME OF THE MEDICINAL PRODUCT**

Fludrocortisonacetat "Galen"

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 50 micrograms of fludrocortisone acetate.

Excipient with known effect

Each tablet contains 93.45 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Tablets

White to off white round flat tablets of approximately 6 mm diameter, embossed with “50” on one side and embossed with ‘FL’ on the other side.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

Fludrocortisonacetat "Galen" tablets 50 micrograms is indicated in infants, children, adolescents and adults for the treatment of:

* Adrenal insufficiency, primary (Addison disease)
* Congenital adrenal hyperplasia, classic (salt-losing adrenogenital syndrome)

**4.2 Posology and method of administration**

Posology

*Adults*

* Adrenal insufficiency, primary (Addison disease): A daily dose of (50)-100-(200) micrograms may be used supplementary to cortisone acetate (usually 12.5 mg, 3 times daily) in cases of insufficient controlled electrolyte balance.

For hypertensive patients a daily dose of 50 micrograms is usually recommended.

* Congenital adrenal hyperplasia, classic (salt-losing adrenogenital syndrome): 100 to 200 micrograms/day.

*Elderly*

No specific dosage recommendations.

*Paediatric population*

*New-borns (during the first year):*

One tablet to four tablets (0.05 to 0.2 mg) 50 to 200 micrograms and exceptionally four to six tablets (0.2 to 0.3 mg) 200 to 300 micrograms.

*Paediatric population (from one year of age):*

One tablet (50 micrograms) to two tablets (100 micrograms) daily. Daily dosage should be adjusted to the age and weight of the child and the severity of the condition (see section 4.4).

*All populations*

The posology should be adjusted according to the blood pressure, the serum potassium and sodium levels and the plasma renin activity, which should be in the normal limit or in the normal upper limit.

Method of administration

For oral use.

In the children below 6 years old, the tablets can be crushed and dissolved, preferably in a fruit juice or in water at ambient temperature and then mixed and administered directly.

**4.3 Contraindications**

* Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
* Hypotension due to organic heart disease,
* Hypokalaemia,
* Metabolic alkalosis,
* All diseases for which an increase in blood pressure or an oedema formation pose an increased risk. This includes i.e., sclerotic vascular changes (e.g., coronary heart disease or cerebral sclerosis, aortic aneurysm, hemodynamically relevant heart valve diseases, heart failure, hypertrophic obstructive cardiomyopathy), cirrhosis of the liver, renal insufficiency, pulmonary oedema, pheochromocytoma.

**4.4 Special warnings and precautions for use**

Fludrocortisone acetate is a potent mineralocorticoid with a glucocorticoid effect which is mainly used for substitution therapy.

Due to the potent mineralocorticoid effect, this medicinal product should not be used in the treatment of disease states other than those mentioned in section 4.1.

Secondary adrenal insufficiency

To avoid secondary adrenal insufficiency, slow tapering is important. To avoid secondary adrenal insufficiency, it may be necessary to increase the dose in case of stress (e.g., fever, trauma, surgery) both during treatment period and up to a year afterwards.

Electrolyte disturbances

The dose and salt intake should be closely monitored to avoid the development of hypertension, oedema or weight gain. Regular check of electrolytes is recommended for long-term treatment. Low sodium diet as well as potassium supplements may be needed.

Protein intake

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

Stress

Patients must be informed about the need for increased dosing in various forms of stress.

Steroid treatment cards

Patients should carry steroid treatment cards which give clear guidance on the precautions to be taken to minimise risk and which provides details of prescriber, drug, dosage and the duration of treatment.

False-negative test results

False negative Nitroblue tetrazolium-test may be obtained.

Beside the mineralocorticoid effects, the following warnings relevant to non-specific glucocorticoid therapy should be taken into account for dosages higher than the ones needed for substitution:

Corticosteroids increase calcium excretion which may predispose to osteoporosis or aggravate pre-existing osteoporosis. Long-term corticosteroid usage may produce rear subcapsular cataract or glaucoma, with a possible damage to the optic nerve. Long-term use may also increase the risk of secondary ocular infections.

Various mental symptoms may occur, e.g. insomnia, euphoria, personality changes, psychoses and depression. The use of antidepressant drugs does not relieve and may exacerbate adrenocorticoid-induced mental disturbances. Menstrual irregularities may occur as well as dyspepsia / ulcer. Corticosteroid effects may be enhanced in patients with hypothyroidism or cirrhosis and decreased in hyperthyroid patients.

Corticosteroids should be used with caution in patients with the following conditions:

Nonspecific ulcerative colitis (if there is a probability of perforation, abscess, or other pyogenic infection); recent intestinal anastomoses; diverticulitis; thromboembolia; thrombophlebitis; existing or previous history of severe affective disorders (especially previous steroid psychosis); exanthematous disease; chronic nephritis or renal insufficiency; metastatic carcinoma; in patients with an active or latent peptic ulcer (or a history of peptic ulcer); myasthenia gravis; hypertension; congestive heart failure; diabetes mellitus; Cushing's disease, cramps.

Infections / vaccinations

Corticosteroids can mask and activate infections.

The response against infection may be weakened and the usual signs of infection may be suppressed. For example, chickenpox, measles, herpes zoster and roundworm (Strongyloides) can have a serious or life-threatening course in non-immune children or patients treated with corticosteroids.

Vaccinations / immunizations should be avoided, especially during treatment with high corticosteroid doses. Neurological complications and lack of antibody response may occur when patients taking corticosteroids are vaccinated.

The use of Fludrocortisonacetat "Galen" tablets in patients with active tuberculosis should be limited to cases of fulminant or disseminated tuberculosis where the corticosteroid is used to treat the disease in combination with the appropriate antituberculosis regimen. Chemoprophylaxis should be used in patients with latent tuberculosis or tuberculin reactivity who are taking corticosteroids.

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

Visual disturbances

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.

Monitoring

Regular monitoring of serum electrolytes, plasma renin activity, blood pressure and clinical signs which may indicate that a dose adjustment (higher or lower) is needed (e.g., oedema, weight gain, high blood pressure, diarrhoea, increased sweating) is recommended.

In new-borns, clinical and biological monitoring (weight, diuresis / electrolytes serum levels) is also recommended.

Doping

Fludrocortisone can be prohibited in competition. Athletes treated with fludrocortisone as replacement therapy should be advised that the product contains an active substance which may produce a positive result in anti-doping tests.

Sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

Lactose

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Paediatric population

Growth and development of children on prolonged corticosteroid therapy should be carefully observed. Prolonged use in children may lead to growth retardation.

Elderly

Monitoring in this patient group is extremely important. Osteoporosis and hypertension may be associated with more serious consequences in the elderly.

**4.5 Interaction with other medicinal products and other forms of interaction**

Fludrocortisonacetat "Galen" tablets may interact with:

Amphotericin B and potassium-depleting agents:

Exacerbated hypokalaemia. Potassium levels should be checked at frequent intervals and potassium supplements used if necessary.

Antidiabetics:

Corticosteroids may increase blood glucose. Patients should be monitored for symptoms of hyperglycaemia; the dose of antidiabetics should be adjusted if necessary.

Anticoagulants, oral:

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

Anticholinesterases:

Effects of anticholinesterase agents may be antagonised.

Barbiturates and other anticonvulsants, phenytoin, carbamazepine, rifampicin:

Increased metabolism of corticosteroids due to hepatic enzyme induction results in increased metabolic clearance of fludrocortisone.

Patients should be monitored for possible diminished effect of steroid and the dose of Fludrocortisonacetat "Galen" tablets should be adjusted accordingly.

Cyclosporin:

Increased effect of both cyclosporine and corticosteroids may occur when the two are used concurrently.

CYP3A inhibitors:

Decreased metabolism of corticosteroids result in increased therapeutic effect. Concomitant treatment with CYP3A inhibitors, including cobicistat-containing medicinal products, is expected to increase the risk of systemic adverse reactions. Combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side effects. Patients should be monitored for systemic corticosteroid side effects.

Digitalis glycosides:

Enhanced risk of arrhythmias and digitalis toxicity associated with hypokalaemia. Potassium levels should be monitored and potassium supplements used if necessary.

Non-depolarizing muscle relaxants:

Corticosteroids may enhance or decrease the neuromuscular blocking action.

Isoniazid:

The serum concentration of isoniazid may be decreased.

Mifamurtide:

Risk of decreased efficacy. Because mifamurtide acts through stimulation of the immune system, the chronic or routine use of corticosteroids should be avoided during treatment with mifamurtide.

NSAID / acetylsalicylic acid:

Corticosteroids may increase the incidence and/or severity of GI bleeding and ulceration associated with NSAIDs. Also, corticosteroids can reduce serum salicylate levels and therefore, decrease their effectiveness. Conversely, discontinuing corticosteroids during high-dose salicylate therapy may result in salicylate toxicity.

Acetylsalicylic acid (Aspirin) should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinaemia.

Somatropin:

The growth-promoting effect may be inhibited.

Thyroid drugs:

Enhanced metabolism of corticosteroids in hyperthyroidism, as well as decreased metabolism in hypothyroidism. Changes in the patient's thyroid status may necessitate a dose adjustment of the adrenocorticoid.

Vaccines:

Risk of neurological complications and lack of antibody response may occur (see section 4.4).

Oestrogen / Birth control pills:

Corticosteroid half-life and concentration may be increased.

A reduction in corticosteroid dosage may be required when oestrogen therapy is initiated, and an increase required when oestrogen therapy is discontinued.

**4.6 Fertility, pregnancy and lactation**

Pregnancy

Treatment during pregnancy should be supervised by a specialist, who has expertise.

There are no or limited amount of data from the use of fludrocortisone acetate in pregnant women.

Corticosteroids have been shown to be teratogenic in some animal species; so far there has been no clear evidence of a similar effect in human beings. Evidence for teratogenicity of fludrocortisone acetate is not available.

As a precautionary measure, it is preferable to avoid the use of fludrocortisone acetate during pregnancy.

Infants born of mothers who have received substantial doses of corticosteroids during pregnancy or during breast feeding should be carefully observed for signs of hypoadrenalism.

Breast-feeding

Fludrocortisone acetate should be used with caution during breast-feeding.

It is not known whether fludrocortisone acetate is excreted in human milk. Corticosteroids are found in breast milk.

Fertility

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

**4.7 Effects on ability to drive and use machines**

No traffic warning.

Fludrocortisone acetate has no or negligible influence on the ability to drive and use machines.

**4.8 Undesirable effects**

Most adverse reactions to fludrocortisone acetate are caused by the drug’s mineralocorticoid activity and include:

* Hypertension, oedema, cardiac enlargement, congestive heart failure, hypokalaemia, hypokalaemic alkalosis.

Despite the occurrence of glucocorticoid adverse reactions, these are not expected at the low dosages being recommended for Fludrocortisonacetat "Galen" tablets. Any adverse reactions may be limited by keeping the dosage as low as possible. However, Fludrocortisonacetat "Galen" tablets are usually used combined with a glucocorticoid, e.g., cortisone.

The list below is presented by system organ class, MedDRA preferred term, and frequency using the following frequency categories:

Very common (≥1/10)

Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1,000 to < 1/100)

Rare (≥ 1/10,000 to < 1/1,000)

Very rare (< 1/10,000)

Not known (cannot be estimated from the available data)

Tabulated list of adverse reactions

|  |
| --- |
| **Immune system disorders** |
| Uncommon (≥1/1,000 and <1/100) | Latent infection activation, e.g., tuberculosis |
| **Endocrine disorders** |
| Uncommon (≥1/1,000 and <1/100) | Symptoms similar to Cushing, activation of latent diabetes mellitus |
| Frequency not known | Adrenal cortex suppression |
| **Metabolism and nutrition disorders** |
| Common - very common (>1/100) | Hypokalaemic alkalosis |
| Uncommon (≥1/1,000 to <1/100) | Growth retardation |
| Very rare (<1/10,000) | Loss of appetite  |
| Frequency not known | Weight loss |
| **Psychiatric disorders** |
| Uncommon (≥1/1,000 to <1/100) | Psychosis, depression, affective symptoms |
| Rare - very rare (<1/1,000) | Hallucinations |
| Frequency not known | Euphoria |
| **Nervous system disorders** |
| Rare - very rare (<1/1,000) | Intracranial hypertension |
| Very rare (<1/10,000) | Headaches, seizures, syncope, taste perversion |
| Frequency not known | Insomnia\*, myasthenia gravis\* |
| **Eye disorders** |
| Uncommon (≥1/1,000 to <1/100) | Glaucoma, rear cataract |
| Frequency not known | Blurred vision, secondary eye infections\* |
| **Cardiac disorders** |
| Common - very common (>1/100) | Heart failure, cardiac enlargement |
| **Vascular disorders** |
| Common - very common (>1/100) | Thrombosis |
| Uncommon (≥1/1,000 and <1/100) | Hypertension |
| **Gastrointestinal disorders** |
| Very rare (<1/10,000) | Diarrhoea  |
| Frequency not known | Dyspepsia/ulcers\* |
| **Skin and subcutaneous tissue disorders** |
| Frequency not known | Skin atrophy, purpura\*, rash\*, petechiae\*, urticaria\* |
| **Musculoskeletal and connective tissue disorders** |
| Common - very common (>1/100) | Weak muscles  |
| Uncommon (≥1/1,000 to <1/100) | Muscle atrophy |
| Frequency not known | Osteoporosis  |
| **Reproductive system and breast disorders** |
| Frequency not known | Menstruation disorders\* |
| **General disorders and administration site conditions** |
| Common - very common (>1/100) | Oedema |
| Frequency not known | Impaired wound healing\* |
| **Investigations** |
| Common - very common (>1/100)  | Hypokalaemia |
| Uncommon (≥1/1,000 and <1/100) | Negative albumin balance  |
| Frequency not known | Hypernatraemia, hypocalcaemia |

\* Adverse effects observed after long-term treatment with fludrocortisone.

Reporting of suspected adverse reactions

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

Lægemiddelstyrelsen

Axel Heides Gade 1

DK-2300 København S

Website: www.meldenbivirkning.dk

**4.9 Overdose**

Overdose has been reported.

Chronic:

*Symptoms*

Hypertension, oedema, hypokalaemia, pronounced weight gain, muscle weakness, cardiac enlargement.

*Management*

Administration of the drug should be discontinued. Subsequent treatment with fludrocortisone acetate, if necessary, should be resumed at a reduced dose. Possibly potassium supplements.

Acute:

Glucocorticoid adverse reactions may occur when overdosing. Blood pressure monitoring as well as a biological monitoring during at least 48 hours is recommended.

Administration of active charcoal is recommended within 4 hours of ingestion.

**4.10 Legal status**

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**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Corticosteroids for systemic use - mineralocorticoids, ATC code: H02AA02.

Fludrocortisone acetate is a synthetic adrenocortical steroid with potent mineralocorticoid effect and high glucocorticoid effect. The medicinal product is used for its mineralocorticoid effect. The glucocorticoid effect is 15 times greater and the mineralocorticoid effect is 125 times greater than that of hydrocortisone. The mechanism of action has not been fully elucidated. Sodium reabsorption in the renal distal tubules and in other tissues appears to account for the physiologic action characteristic of mineralocorticoids. At the same time, the excretion of potassium and hydrogen ions as well as calcium in the urine is increased. Small doses of fludrocortisone acetate result in significant sodium retention, increased urinary potassium excretion and increased blood pressure. In larger doses, endocrine adrenal secretion, thymic activity and pituitary secretion of corticotropin are inhibited. In case of insufficient protein intake, negative nitrogen balance can occur.

Fludrocortisone is used combined with cortisone as a substitution therapy for Addison's disease. For non-tumour induced adrenal cortex hyperplasia there is a decrease of fludrocortisone equal to the 17- ketosteroid excess. Fludrocortisone offers a possibility to diagnose Cushing's syndrome, as its metabolic end products differ from hydrocortisone.

**5.2 Pharmacokinetic properties**

Absorption

The absorption of fludrocortisone is rapid and complete. Following oral ingestion peak plasma concentration occurs after 90 to 120 minutes. The plasma half-life is 3½ hours or more.

Distribution

The volume of distribution is 85 L. Fludrocortisone is 70 to 80 % bound to serum proteins, mainly to globulin fractions.

Biotransformation

Fludrocortisone acetate is rapidly hydrolysed to the active molecule 9a-fluorocortisol. The identified metabolites in human urine are: 9a-Fluoro-3a, 11β, 17a, 20, 21 pentahydroxy-5β-pregnane; 9a-Fluoro-3a, 11β,17a, 20, 21 pentahydroxy-5β-pregnane; 9a-Fluorotetrahydrocortisol; 9a-Fluoroallotetrahydrocortisol; 9a-Fluoro-20,2 0-dihydrocortisol; 9a-Fluoro-11β-hydroxyetiocholanolone and 9a-Fluoro-11β-hydroxyandrostanone.

Elimination

Fludrocortisone acetate is eliminated by the kidneys, mostly as inactive metabolites. Elimination from plasma has been reported to occur in two or three phases with half-lives of 2-3 h, 4.5 h and 10.2 h respectively. Nearly 80 % of 9a-fluorocortisol is eliminated via the urine. The duration of action is 1-2 days.

Special populations

*Renal impairment*

No specific data are available.

*Hepatic impairment*

No specific data are available.

**5.3 Preclinical safety data**

There are not sufficient data to determine whether fludrocortisone acetate is carcinogenic, mutagenic, or impairs fertility in males or females.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Lactose monohydrate

Sodium starch glycolate

Talc (E553b)

Magnesium stearate (E572)

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

30 months.

**6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

**6.5 Nature and contents of container**

Fludrocortisonacetat "Galen" 50 micrograms tablets are packed in OPA/ALU/PVC-alu blisters each of them containing 10 tablets.

Pack sizes: 20, 50 and 100 tablets.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

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

**7. MARKETING AUTHORISATION HOLDER**

GALENpharma GmbH

Wittland 13

24109 Kiel

Germany

**8. MARKETING AUTHORISATION NUMBER(S)**

70745

**9. DATE OF FIRST AUTHORISATION**

3 July 2025

**10. DATE OF REVISION OF THE TEXT**

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