ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Efmody 5 mg modified-release hard capsules
Efmody 10 mg modified-release hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Efmody 5 mg modified-release hard capsules.

Each modified-release hard capsule contains 5 mg hydrocortisone.

Efmody 10 mg modified-release hard capsules.

Each modified-release hard capsule contains 10 mg hydrocortisone.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified-release hard capsules.

Efmody 5 mg modified-release hard capsules.

A capsule (approx.19 mm long) with an opaque blue cap and opaque white body printed with "CHC 5 mg" containing white to off white granules.

Efmody 10 mg modified-release hard capsules.

A capsule (approx.19 mm long) with an opaque green cap and opaque white body printed with "CHC 10 mg" containing white to off white granules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of congenital adrenal hyperplasia (CAH) in adolescents aged 12 years and over and adults.

4.2 Posology and method of administration

Posology

Treatment should be initiated by physicians experienced in the management of CAH.

As maintenance therapy the dose must be individualised according to the response of the individual patient. The lowest possible dose should be used.

Monitoring of the clinical response is necessary and patients should be observed closely for signs that might require dose adjustment, including changes in clinical status resulting from remissions or exacerbations of the disease, changes in electrolytes particularly hypokalaemia (see section 4.4) or hyponatraemia, individual responsiveness to the medicinal product, and the effect of stress (e.g. surgery, infection, trauma). As the treatment has a modified-release profile, blood tests are used to monitor clinical response, assessment of the evening dose should be done with a morning blood test and assessment of the morning dose should be done with an early afternoon blood test.

During excessive physical and/or mental stress it may be necessary to increase the dose of Efmody, and/or add additional immediate release hydrocortisone especially in the afternoon or evening.

Dose adjustments should be considered in case of concomitant use of potent CYP3A4 inducers or inhibitors (see section 4.5).

Treatment in CAH

Recommended replacement doses of hydrocortisone are 10-15 mg/m^2/day in adolescents aged 12 years and over who have not completed growth, and 15-25 mg/day in adolescents who have completed growth and adult patients with CAH. In patients with some remaining endogenous cortisol production a lower dose may be sufficient.

At initiation the total daily dose should be split into two doses with two thirds to three quarters of the dose given in the evening at bedtime and the rest given in the morning. Patients should then be titrated based on their individual response.

The morning dose should be taken on an empty stomach at least 1 hour before a meal and the evening dose taken at bedtime at least 2 hours after the last meal of the day.

Changing from conventional oral glucocorticoid treatment to Efmody

When changing patients from conventional oral hydrocortisone replacement therapy to Efmody, the identical total daily dose should be given, but the dose should be given in two doses with two thirds to three quarters of the dose given in the evening at bedtime and the rest given in the morning.

When changing patients from other glucocorticoids to Efmody an appropriate conversion factor should be used, and the patient monitored for response carefully.

Conversion to Efmody might elicit symptoms of adrenal insufficiency or overreplacement during dose optimisation.

A starting dose exceeding 40 mg per day of hydrocortisone is not recommended.

During serious trauma, intercurrent illness or periods of stress

In severe situations, an increase in dose is immediately required and oral administration of hydrocortisone must be replaced with parenteral treatment (see section 4.4).

In less severe situations when parenteral administration of hydrocortisone is not required, during periods of physical and/or mental stress, additional immediate release hydrocortisone at the same total daily dose as Efmody should be given in three divided doses; Efmody should be continued as well with the usual regimen (i.e. a doubled daily dose of hydrocortisone) to allow for easy return to the normal replacement dose of Efmody once additional hydrocortisone is no longer required.

In case of long-term increases in hydrocortisone daily dose due to prolonged periods of stress or illness, the additional hydrocortisone should be carefully weaned off.

Missed doses

If a dose of Efmody is missed it is recommended that it be taken as soon as possible.

Special populations

Elderly

No clinical data on the safety and efficacy of Efmody are available in elderly patients over the age of 65 years.

Renal impairment

There is no need for dose adjustment in patients with mild to moderate renal impairment. In patients with severe renal impairment monitoring of the clinical response is recommended and adjustment of dose may be necessary (see section 4.4).

Hepatic impairment

There is no need for dose adjustment in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment monitoring of the clinical response is recommended and adjustment of dose may be necessary (see section 4.4).

Paediatric population

No clinical data on the safety and efficacy of Efmody are available in children aged below 12 years. Other hydrocortisone containing medicinal products are available for children below 12 years.

Adolescents

No clinical data on the safety and efficacy of Efmody are available in adolescents aged 12 to 18 years.

Method of administration

The capsules must be given orally.

Patients should be advised to swallow the capsules with water to wash the capsules down.

The capsules should not be chewed as chewing the capsule could affect the release profile.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Adrenal crisis

Acute adrenal insufficiency may develop in patients with known adrenal insufficiency who are on inadequate daily doses or in situations with increased cortisol need. Therefore, patients should be advised of the signs and symptoms of acute adrenal insufficiency and of adrenal crisis and the need to seek immediate medical attention. Sudden discontinuation of therapy with hydrocortisone risks triggering an adrenal crisis and death.

During adrenal crisis parenteral, preferably intravenous administration of hydrocortisone in high doses, together with sodium chloride 9 mg/ml (0.9%) solution for infusion, should be administered according to current treatment guidelines.

Pre-operatively, during serious trauma or during intercurrent illness

Pre-operatively, anaesthetists must be informed if the patient is taking corticosteroids or has previously taken corticosteroids.

Parenteral administration of hydrocortisone is warranted during transient illness episodes such as severe infections, in particular gastroenteritis associated with vomiting and/or diarrhoea, high fever of any aetiology or extensive physical stress, such as for instance serious accidents and surgery under general anaesthesia. Where parenteral hydrocortisone is required, the patient should be treated in a facility with resuscitation facilities in case of evolving adrenal crisis.

In less severe situations when parenteral administration of hydrocortisone is not required, for instance low grade infections, moderate fever of any aetiology and stressful situations such as minor surgical procedures, there should be high awareness of the risk of developing acute adrenal insufficiency.

Infections

Infection should not be more likely at a replacement dose of hydrocortisone, but all infections should be taken seriously, and an increase in steroid dose be initiated early (see section 4.2). Patients with CAH are at risk of life-threatening adrenal crisis during infection so clinical suspicion of infection should be high and specialist advice should be sought early.

Immunisation

Treatment schedules of corticosteroids for people with CAH do not cause immunosuppression and are not, therefore, contraindications for administration of live vaccines.

Undesirable effects of corticosteroid replacement therapy

Most undesirable effects of corticosteroids are dose and duration of exposure related. Undesirable effects are therefore less likely when using corticosteroids as replacement therapy. High (supra-physiological) dosages of hydrocortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium.

Long-term treatment with higher than physiological hydrocortisone doses can lead to clinical features resembling Cushing´s syndrome with increased adiposity, abdominal obesity, hypertension and diabetes, and thus result in an increased risk of cardiovascular morbidity and mortality.
Patients should be warned of the signs of diabetes and the need to seek medical advice if they occur.

All glucocorticoids increase calcium excretion and reduce the bone-remodelling rate. Long-term glucocorticoid replacement therapy may therefore reduce bone mineral density (see section 4.8).

Patients should be warned that potentially severe psychiatric adverse reactions; euphoria, mania, psychosis with hallucinations and delirium have been seen in adult patients at replacement doses of hydrocortisone (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 also 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 should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients 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.

Rare instances of anaphylactoid reactions have occurred in patients receiving corticosteroids, medical advice should be sought immediately in the case of anaphylactoid symptoms (see section 4.8).

Gastric emptying and motility disorders

Modified-release formulations, such as Efmody are not recommended in patients with increased gastrointestinal motility, i.e. chronic diarrhoea, due to the risk of impaired cortisol exposure. There are no data in patients with confirmed slow gastric emptying or decreased motility disease/disorder. The clinical response should be monitored in patients with these conditions.

Growth retardation

Corticosteroids may cause growth retardation in childhood and adolescence; this may be irreversible. Treatment should be limited to the minimum dose required to achieve desired clinical response and when reduction in dose is possible, the reduction should be gradual. Excessive weight gain with decreased height velocity or other symptoms or signs of Cushing syndrome indicate excessive glucocorticoid replacement. Children require frequent assessment to assess growth, blood pressure, and general well-being.

Accelerated sexual maturation

Adolescents with CAH may show accelerated sexual maturation. Patients should be closely monitored; and if signs of early puberty or accelerated sexual maturation are present, an increase in dose should be considered. Careful and regular monitoring of adolescent patients with dose adjustment according to the response of the individual patient is recommended.

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 which have been reported after use of systemic and topical corticosteroids.

Hypokalaemia

Treatment of CAH often warrants additional treatment with mineralocorticosteroids. Potassium should be monitored (see sections 4.5 and 4.8).

Precaution

In both men and women who have lower fertility due to CAH, fertility may be restored shortly after beginning treatment with Efmody, which can lead to unexpected pregnancies. Patients should be informed of the potential for restored fertility when starting treatment with Efmody, to be able to consider if a contraceptive measure is needed (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

Hydrocortisone is metabolised by cytochrome P450 3A4 (CYP3A4). Concomitant administration of medicinal products that are inhibitors or inducers of CYP3A4 may therefore lead to unwanted alterations in serum concentrations of hydrocortisone with the risk of adverse reactions, particularly adrenal crisis. The need for dose adjustment when such medicinal products are used can be anticipated and patients should be closely monitored.

Medicinal products inducing CYP3A4, requiring a potential increase in Efmody dosing, include but are not limited to:

- Anticonvulsants: phenytoin, carbamazepine and oxcarbazepine
- Antibiotics: rifampicin and rifabutin
- Barbiturates including phenobarbital and primidone

- Antiretroviral medicinal products: efavirenz and nevirapine
- Herbal medicinal products such as St. John's Wort

Medicinal products/substances inhibiting CYP3A4, requiring a potential decrease in hydrocortisone dosing, include but are not limited to:

- Anti-fungals: itraconazole, posaconazole, voriconazole
- Antibiotics: erythromycin and clarithromycin
- Antiretroviral medicinal products: ritonavir
- Grapefruit juice
- Liquorice

The desired actions of hypoglycaemic medicinal products including insulin are antagonised by corticosteroids.

Medicinal products/substances that affect the electrolyte balance may increase the risk of hypokalaemia in patients taking Efmody. These include hypokalaemic diuretics, stimulant laxatives, mineralocorticosteroids (fludrocortisone), tetracosactide (Synacthen), IV amphotericin B and liquorice.

4.6 Fertility, pregnancy and lactation

Pregnancy

Hydrocortisone crosses the placenta. Hydrocortisone is preferentially metabolised by placental 11βHSD2 to inactive cortisone reducing the fetal exposure. There are no indications that replacement therapy with hydrocortisone in pregnant women is associated with adverse consequences for the fetus. Hydrocortisone for replacement therapy can be used during pregnancy.
Studies in animals have shown reproductive toxicity of corticosteroids (see section 5.3).

Breast-feeding

Hydrocortisone is excreted in breast milk. However, the doses of hydrocortisone used for replacement therapy probably do not clinically significantly affect the child. Hydrocortisone for replacement therapy can be used during breast-feeding.

Fertility

In both men and women who have lower fertility due to CAH, fertility may be restored shortly after beginning treatment with Efmody. In women, a reduction of 17-OH progesterone and androstenedione will lead to a corresponding fall in progesterone and testosterone which may restore menses/fertility. (see section 4.4).

4.7 Effects on ability to drive and use machines

Efmody has minor influence on the ability to drive and use machines. Fatigue and dizziness have been reported. Untreated and poorly replaced adrenal insufficiency may affect the ability to drive and use machines.

4.8 Undesirable effects

Summary of safety profile

In the clinical trial programme the overall most common serious adverse events were acute adrenal insufficiency (4.2% of patients treated with Efmody), another common adverse reaction, in relation to Efmody was fatigue (11.7% of patients), headache (7.5%), increased appetite (5.8%), dizziness (5.8%)

and increased weight (5.8%). Two serious adverse reactions of hypokalaemia (2.2%) were reported in the long-term extension study DIUR-006 for patients that were receiving a mineralocorticoid.

Tabulated list of adverse reactions

The commonest reactions reported to Efmody in the pooled population in the clinical trial programme, are tabulated below. Frequencies are defined as very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100).

Table 1. Tabulated summary of adverse reactions seen in clinical trial programme

MedDRA system organ classification	**Event**	**Frequency**
Endocrine disorders	Adrenal insufficiency including acute events	Common
Metabolism and nutrition disorders	Increased appetite	Common
	Decreased appetite	Common
	Impaired fasting glucose	Common
Psychiatric disorders	Insomnia	Common
	Abnormal dreams	Common
	Depressed mood	Common
	Sleep disorder	Common
Nervous System Disorders	Headache	Common
	Dizziness	Common
	Carpal tunnel syndrome	Common
	Paraesthesia	Common
Gastrointestinal disorders	Nausea	Common
	Abdominal pain upper	Common
Skin and subcutaneous tissue disorders	Acne	Common
	Hair growth abnormal	Common
Musculoskeletal and connective tissue disorders	Arthralgia	Common
	Muscle fatigue*	Common
	Myalgia	Common
	Pain in extremity	Common
General disorders and administration site conditions	Asthenia	Common
	Fatigue	Very Common
Investigations	Blood potassium decreased	Common
	Low density lipoprotein increased	Common
	Renin increased	Common
	Weight increased	Common

*Includes muscular weakness

Description of selected adverse reactions

Adrenal insufficiency (including acute events).

Events of acute adrenal insufficiency were reported during the clinical trial programme but none were considered related to Efmody. Acute adrenal insufficiency should be monitored for and treated promptly in patients with adrenal insufficiency (see sections 4.2 and 4.4).

Rare instances of anaphylactoid reactions have occurred in patients receiving corticosteroids especially when a patient has a history of allergies to medicinal products.

Historical cohorts of adults treated from childhood for CAH have been found to have reduced bone mineral density and increased fracture rates (see section 4.4) - it is unclear if these relate to hydrocortisone therapy using current replacement regimens.

Historical cohorts of adults treated from childhood for CAH have been found to have raised cardiovascular risk factors and a higher risk of cerebrovascular disease than the general population - it is unclear if these relate to hydrocortisone therapy using current replacement regimens.

Paediatric population

No paediatric patients were included in the clinical development programme for Efmody. Hydrocortisone has been used for more than 60 years in paediatrics with a safety profile similar to that in adults. Growth retardation has been seen in children treated with hydrocortisone for CAH and can be caused by both the disorder and hydrocortisone. Accelerated sexual maturation has been seen in hydrocortisone-treated paediatric CAH patients and is associated with excess adrenal androgen production (see section 4.4).

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 the national reporting system listed in Appendix V.

4.9 Overdose

Reports of acute toxicity and/or deaths following hydrocortisone overdose are rare. No antidote is available. Treatment is probably not indicated for reactions due to chronic poisoning unless the patient has a condition that would render him/her unusually susceptible to ill effects from hydrocortisone. In which case, symptomatic treatment should be instituted as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids for systemic use; glucocorticoids. ATC code: H02AB09.

Mechanism of action

Hydrocortisone is a glucocorticoid. Glucocorticoids have multiple effects in multiple tissues through actions on the intracellular steroid receptors.

Pharmacodynamic effects

Hydrocortisone is a glucocorticoid and the synthetic form of endogenously produced cortisol. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastro-intestinal tract. Cortisol is the principal corticosteroid secreted by the adrenal cortex. Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. They are also used for their potent anti-inflammatory effects in disorders of many organ systems. Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

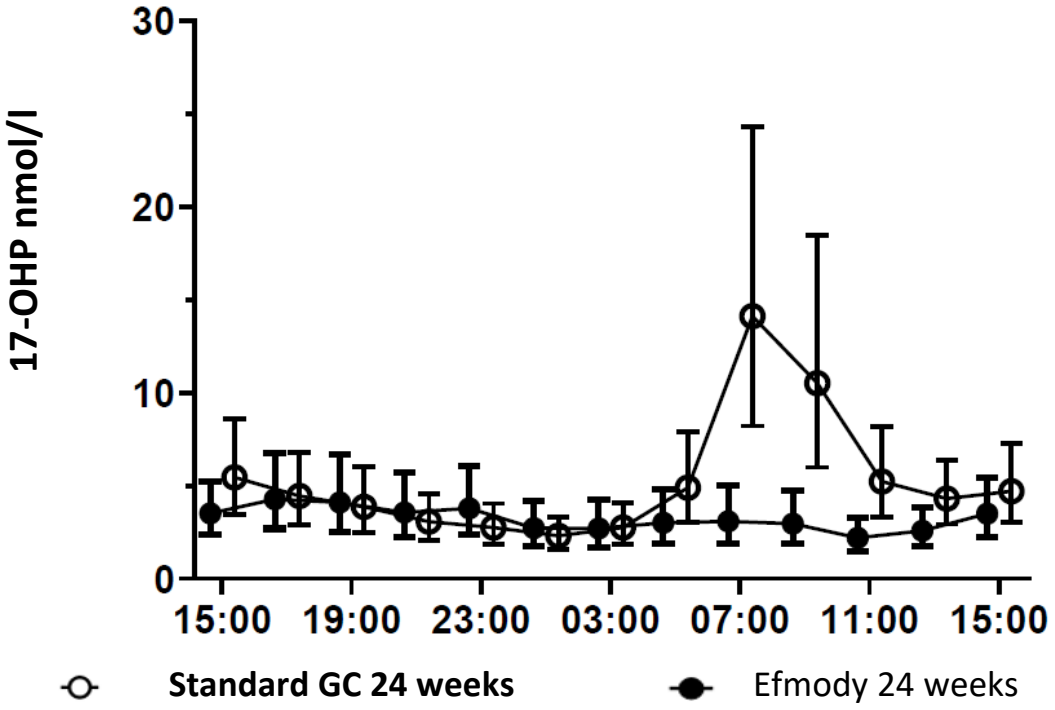
Clinical efficacy and safety

A study in 122 participants with genetically diagnosed 21-hydroxylase deficiency randomised to Efmody or continuation of standard care with blinded titration of dose and regular overnight profiles failed to meet its primary endpoint of superiority in change from baseline to 24 weeks of the mean of the 24-hour standard deviation score (SDS) profile for 17-hydroxyprogesterone 17-OHP. The 17-OHP SDS was lower in the Efmody cohort than standard therapy at 4 and 12 weeks. At 24 weeks the 17-OHP SDS was lower in the morning period (07:00 hrs to 15:00 hrs) but not in the evening or overnight (see also Figure 1 for the geometric mean 24-hour profile of 17-OHP after 24 weeks intensive treatment). A reduction in the 17-OHP area under the curve occurred in both groups, with greater reduction in the Efmody cohort. The percentage of patients with controlled 09:00 hrs 17-OHP (<36nmol/l) was 50% at baseline and at 24 weeks was 91% in the Efmody cohort and 71% in the standard therapy cohort. Efmody patients suffered no adrenal crises (compared to 3 in the control arm) and had fewer sick day episodes where increased dosing due to stress was required (26 vs 36 in the control arm) despite reporting more episodes of intercurrent infective or gastro-intestinal illness. Glucocorticoid daily dose, measured as a hydrocortisone equivalent dose, increased in most subjects during the study (see Table 2).

Table 2. Glucocorticoid daily dose changes during the phase 3 study DIUR-005

Dose	**Hydrocortisone modified-release hard capsules group**		**Standard glucocorticoid group**	
	Baseline	**24 weeks**	**Baseline**	**24 weeks**
All (hydrocortisone dose equivalents)				
Median daily dose (mg)	25.0	30.0	25.0	31.3
On hydrocortisone at baseline				
Median daily dose (mg)	20.0	25.0	23.75	25.0
On prednis(ol)one at baseline				
Median daily dose (mg)	30	27.5	26.6	32.8
On dexamethasone at baseline				
Median daily dose (mg)	30	30	40	40

Figure 1. End of study geometric mean 24-hour profile of 17-OHP after 24 weeks intensive treatment with either Efmody (closed circles) or standard therapy (open circles).



A safety extension study of 91 patients with titration by investigators (DIUR-006) was characterised by dose reductions with median daily dose of Efmody at 18 months interim analysis (n=50) being 20 mg (from a median baseline daily dose of 30 mg) with 17-OHP levels remaining in the clinically determined optimal range and androstenedione at or below the reference range for normal individual.

In the safety assessment of clinical studies, differences between the treatment arms in treatment related AEs were reported (by preferred term [PT]). The most notable differences between the Efmody and standard glucocorticoid therapy pools, respectively, were observed for headache (7.5% vs 1.6%), increased appetite (5.8% vs 3.3%), weight increase (including abnormal weight gain) (9.2% vs1.6%), decreased appetite (5.0% vs 0%) and nausea (4.2% vs 1.6%).

5.2 Pharmacokinetic properties

Absorption

Following a single oral administration in fasted dexamethasone-suppressed healthy adults, the rate of absorption of hydrocortisone from Efmody 20 mg was delayed and reduced compared to immediate release hydrocortisone tablets 20 mg, as reflected by a lower C_{max} and a significantly longer T_{max} for Efmody (median T_{max} for serum cortisol of 4.5 hours and 0.88 hours for Efmody and hydrocortisone tablets respectively). Efmody appeared to be more bioavailable relative to immediate release hydrocortisone tablets, with overall exposure to serum cortisol and derived free cortisol approximately 19% and 13% higher respectively for Efmody.

In the same population, food (high fat meal started 30 minutes before dosing) was found to delay and reduce the rate of absorption of hydrocortisone from Efmody 20 mg, as reflected by a longer T_{max}

(median T_{max} for serum cortisol of 6.75 hours and 4.5 hours for fed and fasted subjects respectively) and lower C_{max} (reduced by approximately 20% in fed subjects). Overall exposure appeared similar in fed and fasted subjects (90% confidence intervals for the fed/fasted ratio of the geometric least square mean of AUC_{0-t} and AUC_{0-inf} were within 80-125%). This effect is therefore not considered clinically significant.

Distribution

90% or more of circulating hydrocortisone is reversibly bound to protein.

The binding is accounted for by two protein fractions. One, corticosteroid-binding globulin is a glycoprotein; the other is albumin.

Biotransformation

Hydrocortisone is metabolised in the liver and most body tissues to hydrogenated and degraded forms such as tetrahydrocortisone and tetrahydrocortisol which are excreted in the urine, mainly conjugated as glucuronides, together with a very small proportion of unchanged hydrocortisone. Hydrocortisone is both metabolised by and a regulator of CYP3A4.

Elimination

In the fasted dexamethasone-suppressed healthy adult population described above, terminal elimination half-life values were similar for Efmody and hydrocortisone tablets (geometric mean $t_{1/2}$ for serum cortisol of 1.38 hours and 1.40 hours respectively). Clearance appeared higher for hydrocortisone tablets relative to Efmody (geometric mean CL/F for serum cortisol of 22.24 L/h and 18.48 L/h respectively).

Paediatrics

The pharmacokinetics of Efmody have not been studied in the paediatric population.

Other populations

No studies have been conducted in patients with hepatic or renal impairment.

5.3 Preclinical safety data

Administration of corticosteroids to pregnant animals can cause abnormalities of fetal development including cleft palate, intrauterine growth retardation and effects on brain growth and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Granules

Microcrystalline cellulose
Povidone
Methacrylic acid-methyl methacrylate copolymer (1:2)
Methacrylic acid-methyl methacrylate copolymer (1:1)
Talc
Dibutyl sebacate

Capsule

Gelatin

Efmody 5 mg modified-release hard capsules (white/blue)

Titanium dioxide (E171)
Indigotine (E132)

Efmody 10 mg modified-release hard capsules (white/green)

Titanium dioxide (E171)
Indigotine (E132)
Yellow iron oxide (E172)

Printing ink

Shellac
Black iron oxide (E172)
Propylene glycol
Potassium hydroxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container

The capsules are provided in high-density polyethylene bottles with child resistant, tamper-evident polypropylene screw cap with integrated desiccant. Each bottle contains 50 modified-release hard capsules.

Pack size:
Carton containing 1 bottle of 50 modified-release hard capsules.
Carton containing 2 bottles of 50 modified-release hard capsules (100 capsules).

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

Neurocrine Netherlands B.V.
Van Heuven Goedhartlaan 935 A,
1181LD Amstelveen,
The Netherlands
diurnalinfo@neurocrine.com

8. MARKETING AUTHORISATION NUMBER(S)

Efmody 5 mg modified-release hard capsules	EU/1/21/1549/001 (50 capsules)
Efmody 10 mg modified-release hard capsules	EU/1/21/1549/002 (50 capsules)
Efmody 5 mg modified-release hard capsules	EU/1/21/1549/004 (100 (2x50) capsules)
Efmody 10 mg modified-release hard capsules	EU/1/21/1549/005 (100 (2x50) capsules)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 May 2021

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release
Skyepharma Production SAS
Zone Industrielle Chesnes Ouest
55 rue du Montmurier
Saint Quentin Fallavier, 38070
France

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (See Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c (7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency.
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON 5 MG HARD CAPSULES - 50 CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Efmody 5 mg modified-release hard capsules
hydrocortisone.

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release hard capsules

50 modified-release hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Neurocrine Netherlands B.V.Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1549/001 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Efmody 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL 5 MG HARD CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Efmody 5 mg modified-release hard capsules
hydrocortisone.

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release hard capsules

50 modified-release hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Neurocrine Netherlands B.V.Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1549/001 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON 10 MG HARD CAPSULES - 50 CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Efmody 10 mg modified-release hard capsules
hydrocortisone**.**

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 10 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release hard capsules

50 modified- release hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Neurocrine Netherlands B.V.Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1549/002 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Efmody 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL 10 MG HARD CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Efmody 10 mg modified-release hard capsules
hydrocortisone**.**

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 10 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release hard capsules

50 modified-release capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Neurocrine Netherlands B.V.Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1549/002 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON 5 MG HARD CAPSULES - 100 (2X50) CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Efmody 5 mg modified-release hard capsules
hydrocortisone.

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release hard capsules

100 (2x50) modified-release hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Neurocrine Netherlands B.V.Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1549/004 100 (2x50) capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Efmody 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON 10 MG HARD CAPSULES - 100 (2X50) CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Efmody 10 mg modified-release hard capsules
hydrocortisone**.**

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 10 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release hard capsules

100 (2x50) modified- release hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Neurocrine Netherlands B.V.Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1549/005 100 (2x50) capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Efmody 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Efmody 5 mg modified-release hard capsules
Efmody 10 mg modified-release hard capsules
hydrocortisone

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Efmody is and what it is used for

Medicine contains the active substance hydrocortisone. Hydrocortisone belongs to a group of medicines known as corticosteroids.

Hydrocortisone is a copy of the hormone cortisol. Cortisol is made by the adrenal glands in the body. Efmody is used when the adrenal gland are not making enough cortisol due to an inherited condition called congenital adrenal hyperplasia. It is for use in adults and adolescents from 12 years of age.

2. What you need to know before you take Efmody

Do not take Efmody
- If you are allergic to hydrocortisone or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking Efmody if the following apply:

Adrenal crisis
- You have an adrenal crisis. If you are vomiting or seriously unwell, you may need an injection of hydrocortisone. Your doctor will train you how to do this in an emergency.

Infections
- You have an infection or you do not feel well. Your doctor may need to prescribe extra hydrocortisone temporarily.

Immunisation
- You are due to be vaccinated. Usually, taking Efmody should not stop you receiving vaccination.

Fertility
- If you had lower fertility due to congenital adrenal hyperplasia, your fertility may be restored, sometimes soon after starting Efmody. This applies to both men and women. Talk to your doctor about your contraceptive needs before starting Efmody.

Other
- You are due for an operation. Tell the surgeon or anaesthetist that you are receiving Efmody before your operation.
- You have a long-term condition of your digestive system (such as chronic diarrhoea) that affects how well your gut absorbs food. Your doctor may prescribe another medicine instead or monitor you more closely to check that you are getting the right amount of the medicine.

You should not stop taking Efmody without checking with your doctor as this could make you seriously unwell very quickly.

As Efmody is replacing the normal hormone your body lacks, side effects are less likely, however:

- Too much Efmody can affect your bones so your doctor will monitor the dose closely.

- Some patients taking hydrocortisone Efmody became anxious, depressed or confused.Tell your doctor if you develop any unusual behaviour or feel suicidal after starting medication (see section 4).

- In rare cases allergy to hydrocortisone can occur. People who already have allergies to other medicines may be more likely to develop allergy to hydrocortisone.Tell your doctor straight away if you have any reaction like swelling or shortness of breath after being given Efmody (see section 4).

- High doses of hydrocortisone can increase the risk of heart disease and circulatory problems by causing raised blood pressure, salt and water retention, obesity and diabetes. If you have symptoms of excessive thirst or need to pass urine excessively tell your doctor straight away.

- Treatment with steroids can lead to low blood potassium (hypokalaemia). See section 4. Your doctor will monitor your potassium levels to check for any changes.

- Hydrocortisone can reduce growth in children.Your doctor will monitor your growth while you are on Efmody.

- Children with congenital adrenal hyperplasia taking hydrocortisone might show signs of sexual development or puberty earlier than usually expected. Your doctor will monitor your development while you are on Efmody.

- Contact your doctor if you have blurred vision or other visual disturbances.

Other medicines and Efmody
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines can affect the way that Efmody works and may mean that your doctor needs to alter your dose of Efmody.

Your doctor may need to increase your dose of Efmody if you take certain medicines, including:
- Medicines used to treat epilepsy: phenytoin, carbamazepine, oxcarbazepine and barbiturate medicines such as phenobarbital and primidone.
- Medicines used to treat infections (antibiotics): rifampicin and rifabutin.
- Medicines used to treat human immunodeficiency virus (HIV) infection and AIDS: efavirenz and nevirapine.
- Herbal medicine used to treat depression e.g. St. John's wort.

Your doctor may need to decrease your dose of Efmody if you take certain medicines including:
- Medicines used to treat fungal diseases: itraconazole, posaconazole, and voriconazole.
- Medicines used to treat infections (antibiotics): erythromycin and clarithromycin.
- Medicine used to treat human immunodeficiency virus (HIV) infection and AIDS: ritonavir.

If you are taking medicines that can lower your potassium levels, your risk of developing hypokalaemia (low potassium) will be higher than when taking Efmody alone and will be monitored by your doctor. These medicines include:
- Medicines used to maintain sodium (salt) levels: mineralocorticoids, such as fludrocortisone.
- Medicines used to reduce fluid content: diuretics.
- Medicines used to increase bowel movement: stimulant laxatives.
- Medicines used to treat infections (antibiotics): amphotericin B
- Medicines used to test the adrenal gland: Synacthen or tetracosactide.

Efmody with food and drink
Some food and drink may affect the way Efmody works and may need your doctor to decrease your dose. These include:
- Grapefruit juice.
- Liquorice. (This may also lower your potassium levels).

Pregnancy, breast-feeding and fertility
Hydrocortisone is known to cross the placenta in pregnancy and is present in breast milk, however there is no evidence this causes any harm to the infant. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

If you are a woman who has not gone through menopause your periods might return or become more regular. The restored fertility may lead to unexpected pregnancy even before the reoccurrence of menstrual bleeding. See also section “Warnings and precautions” regarding fertility in both men and women.

Driving and using machines
Efmody has minor influence on the ability to drive and use machines. Untreated adrenal insufficiency may affect the ability to drive and use machines. Tell your doctor immediately if you feel tired or dizzy when taking Efmody.

3. How to take Efmody

Always use this medicine exactly as your doctor, nurse or pharmacist has told you. Check with them if you are not sure.

Your doctor will decide on the right starting dose of Efmody and then adjust the dose as needed depending on the severity of your disease, how well you respond to Efmody and any changes in your condition, using blood tests to measure the effect on your adrenal gland and also to check your sodium and potassium levels.. During illnesses, around the time of surgery and during times of serious stress, your doctor may ask you to take another corticosteroid medicine instead of, or as well as, Efmody.

The initial daily dose may be divided into 2 doses with two thirds to three quarters of your daily dose in the evening at bedtime and the rest given in the morning.

The morning dose of hydrocortisone modified-release hard capsules should be taken on an empty stomach at least 1 hour before a meal and the evening dose taken at bedtime at least 2 hours after the last meal of the day.

Use in Children
No information on the safety and efficacy of Efmody in children under 12 years is available. Other hydrocortisone containing medicines are available for children under 12 years.

How to take this medicine
Swallow the capsules with water .
Do not chew the capsules as it could change the release of the medicine.

If you take more Efmody than you should
If you take more Efmody than you should, contact your doctor or pharmacist for further advice as soon as possible.

If you forget to take Efmody
If you forget to take a dose, take the dose as soon as possible.

If you stop taking Efmody
Do not stop taking Efmody without asking your doctor first. Stopping the medicine suddenly could quickly lead to an adrenal crisis.

If you become unwell
Tell your doctor or pharmacist if you become ill, suffer severe stress, get injured or are about to have surgery because your doctor may advise that you take another corticosteroid medicine instead of, or as well as, Efmody (see section 2).

If you take too much Efmody
Poisoning or death are rare with too much Efmody, but you should inform your doctor immediately.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

- If you have any reaction like swelling or shortness of breath after taking Efmody, get medical help straight away and tell your doctor as soon as possible as these can be signs of an severe allergic reaction (anaphylactoid reactions) (see section 2).

- Adrenal crisis and adrenal insufficiency symptoms have been reported commonly (may affect up to 1 in 10 people). If you get less hydrocortisone than you need you may become seriously unwell. If you feel unwell and particularly if you start vomiting you must tell your doctor straight away as you may need extra hydrocortisone or an injection of hydrocortisone.

Tell your doctor about any of the following side effects as soon as possible:

Very Common (may affect more than 1 in 10 people)
- Tiredness

Common (may affect up to 1 in 10 people)
- Feeling sick (nausea)
- Belly (abdominal) pain
- Loss of energy or weakness
- Increased or decreased appetite and weight gain or loss
-
- Muscle pains and weakness
- Joint pains
- Headache
- Dizziness
- Pain or tingling in the thumb or fingers (carpal tunnel syndrome)
- Tingling
- Insomnia, sleep difficulties or unusual dreams
- Depressed mood
- Acne
- Hair growth
- Changes in blood tests of kidney and glucose
- Changes in blood tests of low density lipoprotein (raised LDL-cholesterol)
- Changes in blood tests of potassium (hypokalaemia or low potassium)

Long-term treatment with hydrocortisone may reduce bone density. Your doctor will monitor your bones (see section 2).

People who require treatment with steroids may have a higher risk of heart disease. Your doctor will monitor you for this.

Long term treatment with hydrocortisone can affect growth in children and young people. Your doctor will monitor your growth in young people. Some children with congenital adrenal hyperplasia treated with hydrocortisone can have an earlier puberty than expected. Your doctor will monitor your development (see section 2).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Efmody

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and carton after EXP. The expiry date refers to the last day of that month.

This medicine does not have any special temperature storage requirements.

Store in the original package.

Keep the bottle tightly closed in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Efmody contains

- The active substance is hydrocortisone
    - Efmody 5 mg modified-release hard capsules: each modified-release capsule contains 5 mg of hydrocortisone
    - Efmody 10 mg modified-release hard capsules: each modified-release capsule contains 10 mg of hydrocortisone
-
- The other ingredients are microcrystalline cellulose, povidone, methacrylic acid-methyl methacrylate copolymer, talc, and dibutyl sebacate.

Capsule
The capsule is made from gelatin.

Efmody 5 mg modified-release hard capsules (white/blue)
Titanium dioxide (E171) and indigotine (E132)

Efmody 10 mg modified-release hard capsules (white/green)
Titanium dioxide (E171), indigotine (E132) and yellow iron oxide (E172)

Printing ink
The printing ink on the capsules contains shellac, black iron oxide (E172), propylene glycol and potassium hydroxide

What Efmody looks like and contents of the pack

- Efmody 5 mg modified-release hard capsules
  A capsule (approx.19 mm long) with an opaque blue cap and opaque white body printed with "CHC 5mg" containing white to off white granules.

- Efmody 10 mg modified-release hard capsules
  A capsule (approx.19 mm long) with an opaque green cap and opaque white body printed with "CHC 10mg" containing white to off white granules.

Efmody comes in a high density polyethylene bottles with child resistant, tamper-evident polypropylene screw cap with integrated desiccant. Each bottle contains 50 modified-release hard capsules.

Pack size:
Carton containing 1 bottle of 50 modified-release hard capsules.
Carton containing 2 bottles of 50 modified-release hard capsules (100 capsules).

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Neurocrine Netherlands B.V.
Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
The Netherlands
diurnalinfo@neurocrine.com

Manufacturer
Skyepharma Production SAS
Zone Industrielle Chesnes Ouest
55 rue du Montmurier
Saint Quentin Fallavier, 38070
France

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
https://www.ema.europa.eu