ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 0.5 mg granules in capsules for opening
Alkindi 1 mg granules in capsules for opening
Alkindi 2 mg granules in capsules for opening
Alkindi 5 mg granules in capsules for opening

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Alkindi 0.5 mg granules in capsules for opening

Each capsule contains 0.5 mg hydrocortisone.

Alkindi 1 mg granules in capsules for opening

Each capsule contains 1 mg hydrocortisone.

Alkindi 2 mg granules in capsules for opening

Each capsule contains 2 mg hydrocortisone.

Alkindi 5 mg granules in capsules for opening

Each capsule contains 5 mg hydrocortisone.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Granules in capsules for opening.

The granules are white to off-white and contained in a transparent colourless (size 00el) hard capsule.

Alkindi 0.5 mg granules in capsules for opening

The capsule is printed with "INF-0.5" in red ink.

Alkindi 1 mg granules in capsules for opening

The capsule is printed with "INF-1.0" in blue ink.

Alkindi 2 mg granules in capsules for opening

The capsule is printed with "INF-2.0" in green ink.

Alkindi 5 mg granules in capsules for opening

The capsule is printed with "INF-5.0" in grey ink.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy of adrenal insufficiency in infants, children and adolescents (from birth to < 18 years old).

4.2 Posology and method of administration

Posology

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, individual responsiveness to the medicinal product, and the effect of stress (e.g. surgery, infection, trauma). During stress it may be necessary to increase the dose temporarily.

Replacement therapy in primary and secondary adrenal insufficiency

Alkindi is given as replacement therapy by oral administration of granules according to clinical practice, in a dose to be titrated against individual clinical response.

Recommended replacement doses of hydrocortisone are 8-10 mg/m^2/day for patients with adrenal insufficiency alone and 10-15 mg/m^2/day in patients with congenital adrenal hyperplasia (CAH), typically in three or four divided doses.

In patients with some remaining endogenous cortisol production a lower dose may be sufficient.

In situations when the body is exposed to excessive physical and/or mental stress, patients may need an increased dose, especially in the afternoon or evening.

Pre-operatively, during serious trauma or illness in patients with known adrenal insufficiency or doubtful adrenal reserve

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

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, and the normal oral daily replacement dose should be increased temporarily; the Alkindi total daily dose should be increased by doubling or tripling the usual dose. Once the intercurrent illness episode is over, patients can return to the normal replacement dose of Alkindi.

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

Changing from conventional oral glucocorticoid treatment to Alkindi

When changing patients from conventional oral hydrocortisone replacement therapy, crushed or compounded, to Alkindi, an identical total daily dose may be given. Alkindi is therapeutically equivalent to conventional oral hydrocortisone formulations. Where a patient is changed from other oral hydrocortisone formulations to Alkindi, inaccuracy in the dosing possible with other oral hydrocortisone formulations can lead to a relative fall in hydrocortisone exposure on the same nominal dose, leading to symptoms of adrenal insufficiency or crisis (see section 4.4).

Missed or Incomplete Dose

If a full dose of Alkindi is missed, that dose should be administered as soon as possible, as well as their next dose at the usual time, even if this means that the child receives two doses at the same time.

Patients and/or caregivers should be instructed to contact their healthcare provider if most of the granules in a dose are regurgitated, vomited or spat out, as a repeat dose may be required to avoid adrenal insufficiency.

Method of administration

The granules must be given orally and should not be chewed. The capsule shell must not be swallowed but carefully be opened as follows:

- The capsule is held so that the printed strength is at the top, and tapped to ensure all the granules are in the lower half of the capsule.
- The bottom of the capsule is gently squeezed.
- The top of the capsule is twisted off.
- The granules are either poured directly onto the child's tongue, or the granules are poured onto a spoon and placed in the child's mouth. For children who are able to take soft food, the granules may be sprinkled onto a spoonful of cold or room temperature soft food (such as yoghurt or fruit puree) and given immediately.
- Whichever method is used, the capsule is tapped to ensure all the granules are removed.

Immediately after administration a drink such as water, milk, breast-milk, or formula-milk should be given to help ensure all granules are swallowed.

If the granules are sprinkled onto a spoonful of soft food this should be given immediately (within 5 minutes) and not stored for future use.

The granules must not be added to liquid as this can result in less than the full dose being given, and may affect the taste masking which will allow the bitter taste of hydrocortisone to become apparent.

Do not administer via nasogastric tube as there is a risk of nasogastric tube blockage (see section 4.4).

Detailed pictograms on how to administer the granules are provided in the package leaflet.

4.3 Contraindications

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

Patients with dysphagia or premature infants where oral feeding has not been established.

4.4 Special warnings and precautions for use

Adrenal crisis

Where a child is vomiting or acutely unwell parenteral hydrocortisone should be started without delay, carers should be trained in adminstering this in an emergency.

Sudden discontinuation of therapy with hydrocortisone risks triggering an adrenal crisis and death. Medicinal product-induced secondary adrenocortical insufficiency may result from too rapid a withdrawal of corticosteroids and may be minimised by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, corticosteroid therapy should be reinstated.

Adrenal crisis can occur when switching from conventional oral hydrocortisone formulations, crushed or compounded, to Alkindi. Close monitoring of patients is recommended in the first week after switch. Healthcare professionals should inform carers and patients that extra doses of Alkindi should be given if symptoms of adrenal insufficiency are seen. If this is required, then an increase in the total daily dose of Alkindi should be considered and immediate medical advice should be sought.

Immunisation

Replacement schedules of corticosteroids for people with adrenal insufficiency do not cause immunosuppression and are not, therefore, contraindications for administration of live vaccines.

Infections

Infection should not be more likely at a replacement dose of hydrocortisone, but all infections should be treated seriously and stress dosing of steroid initiated early (see section 4.2). Patients with adrenal insufficiency 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.

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.

Corticosteroids may cause growth retardation in infancy, 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. Infants require frequent assessment and should be evaluated at a minimum every 3 to 4 months to assess growth, blood pressure, and general well-being.

Bone mineral density may be impacted in children when higher doses of replacement steroids are used. The lowest appropriate dose of steroid according to the response of the individual patient should be used.

Patients/and or carers 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/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately

after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

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

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.

Excretion of granules

The granules may sometimes be seen in stools since the centre of the granule is not absorbed in the gut after it has released the active substance. This does not mean the medicinal product has been ineffective and the patient should not take another dose for this reason.

Nasogastric tube feeding

Alkindi granules are not suitable for nasogastric administration as they may cause tube blockage.

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 Alkindi 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 Alkindi 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

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

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Hydrocortisone for replacement therapy can be used during pregnancy. 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.

Studies in animals have shown reproductive toxicity of corticosteroids (see section 5.3)

Breast-feeding

Hydrocortisone for replacement therapy can be used during 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.

Fertility

There are no data available for possible effects of Alkindi on fertility.

4.7 Effects on ability to drive and use machines

Alkindi has no or negligible influence on the ability to perform skilled tasks (e.g. riding a bicycle) or using machines.

4.8 Undesirable effects

Summary of safety profile

A total of 30 healthy (but dexamethasone-suppressed) adult male subjects in two phase 1 studies and 24 paediatric patients with adrenal insufficiency in two phase 3 studies have been treated with Alkindi. There were no adverse reactions and no episodes of adrenal crisis seen in any of the studies.

In clinical practice most adverse reactions have been mild and self-limiting but adrenal crisis has been observed at time of changing from other hydrocortisone products and monitoring of patients at time of switch is advised (see section 4.4).

Tabulated list of adverse reactions

The following adverse reactions have been reported in the scientific literature in adult patients for other hydrocortisone medicinal products when given as adrenal insufficiency replacement therapy with frequency not known (cannot be estimated from the available data).

Table 1 – Adverse reactions

MedDRA system organ class	Frequency: not known
Psychiatric disorders	Psychosis with hallucinations and delirium Mania Euphoria
Gastrointestinal disorders	Gastritis Nausea
Renal and urinary disorders	Hypokalaemic alkalosis

Description of selected adverse reactions

When changing a patient from other oral hydrocortisone formulations to Alkindi, inaccuracy in the dosing possible with other oral hydrocortisone formulations can lead to a relative fall in hydrocortisone exposure on the same nominal dose, leading to symptoms of adrenal insufficiency such as tiredness, excessive sleeping, poor feeding, or adrenal crisis (see section 4.4).

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

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.

The biological half-life of hydrocortisone is about 100 minutes.

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 are adrenocortical steroids, both naturally-occurring and synthetic, which are readily absorbed from the gastro-intestinal tract.

Pharmacodynamic effects

Hydrocortisone is believed to be 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

Paediatric population
The pivotal study was an open-label single-dose single-centre trial in 24 paediatric patients aged less than 6 years requiring replacement therapy for adrenal insufficiency due to CAH, primary adrenal failure or hypopituitarism. The study consisted of three consecutive cohorts, the first including 12 patients aged 2 to less than 6 years, the second including 6 patients aged 28 days to less than 2 years, and the third including 6 neonates aged from birth to less than 28 days.

Of these 24 patients, 23 had a diagnosis of CAH and 1 had a diagnosis of hypopituitarism including hypothyroidism. 1 patient had renal hypoplasia, 1 patient atopic dermatitis and 1 patient had rhinitis. The study used a single dose of Alkindi granules equivalent to the previous morning's dose of each patient's usual glucocorticoid treatment. The Alkindi dose range administered was 1 mg - 4 mg. Parents/carers (and where possible children) assessed the palatability of Alkindi after administration using a 5-item Likert scale.

As this was a single-dose study, the primary efficacy assessment was serum cortisol at 60 minutes. In all 24 patients Alkindi was found to increase cortisol values from baseline as expected: median baseline cortisol 14.1 nmol/l (range 14.1 - 104.5), median C_{max} 535.2 nmol/l (range 346.2 - 1445.1).

Alkindi was positively assessed in terms of palatability. Among parents and carers asked about their child's experience of taking the medication (n=23), 82.6% agreed/strongly agreed that their child found swallowing Alkindi easy; 65.2% agreed/strongly agreed that their child showed a positive reaction after Alkindi administration; 95.5% would be happy to give their child Alkindi in the future; and 95.5% said that they would prefer Alkindi for their child's treatment over their usual hydrocortisone formulation. Six of the 12 children in Cohort 1 (age range 2.6 to 4.7 years) responded to an adjusted palatability questionnaire. ≥50% subjects reported that the taste, feel in mouth and ease of swallowing were very good and that they were likely to take the medicinal product again. 68.8% of healthy adult volunteers have described the taste as neutral.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, hydrocortisone is rapidly absorbed from the gastro-intestinal tract and the oral Alkindi 4x5 mg was approximately 87% bioavailable when compared to intravenous hydrocortisone in dexamethasone-suppressed healthy adult male volunteers.

The coadministration of Alkindi with soft food (yoghurt and fruit puree) has been studied *in vitro* with no significant effect on dissolution seen.
An *in vivo* study in healthy volunteers showed no significant difference in overall exposure when Alkindi was dosed fed or fasted.

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.

The terminal half-life of hydrocortisone is about 1.5 hours following intravenous and oral dosing of hydrocortisone tablets and Alkindi in dexamethasone-suppressed healthy adult male volunteers.

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
Hypromellose
Magnesium stearate
Ethyl cellulose

Capsule

Hypromellose

Printing ink

Shellac
Propylene glycol
Concentrated ammonia solution

Alkindi 0.5 mg capsules (red ink)

Red iron oxide (E172)
Potassium hydroxide

Alkindi 1 mg capsules (blue ink)

Indigotine (E132)

Alkindi 2 mg capsules (green ink)

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

Alkindi 5 mg capsules (grey ink)

Titanium dioxide (E171)
Black iron oxide (E172)
Potassium hydroxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

After first opening: 60 days.

6.4 Special precautions for storage

Do not store above 30°C. Store in the original bottle in order to protect from light.

6.5 Nature and contents of container

The capsules are provided in high-density polyethylene bottles with polypropylene closure with integrated desiccant.

Pack size:
1 bottle containing 50 capsules

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)

EU/1/17/1260/001
EU/1/17/1260/002
EU/1/17/1260/003
EU/1/17/1260/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 February 2018
Date of latest renewal: 09 November 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicine is available on the European Medicines Agency web site: http://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(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Delpharm Lille SAS
Parc d'Activités Roubaix-Est
22 rue de Toufflers CS 50070
Lys Lez Lannoy, 59 452
France

Wasdell Europe Limited
IDA Dundalk Science and Technology Park
Mullagharlin
Dundalk
Co. Louth, A91 DET0
Ireland

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 medical prescription.

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 0.5 MG CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 0.5 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 0.5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

Open date:

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/001 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Alkindi 0.5 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 0.5 MG CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 0.5 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 0.5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/001 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 1 MG CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 1 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 1 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

Open date:

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/002 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Alkindi 1 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 1 MG CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 1 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 1 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/002 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 2 MG CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 2 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 2 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

Open date:

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/003 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Alkindi 2 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 2 MG CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 2 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 2 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/003 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 CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 5 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

Open date:

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/004 50 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Alkindi 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 CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Alkindi 5 mg granules in capsules for opening
hydrocortisone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 5 mg hydrocortisone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Granules in capsules for opening

50 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

Do not swallow the capsule, risk of choking.

8. EXPIRY DATE

EXP

Use capsules within 60 days once the bottle is opened.

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C. Store in the original bottle in order to protect from light.

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/1/17/1260/004 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

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Alkindi 0.5 mg granules in capsules for opening
Alkindi 1 mg granules in capsules for opening
Alkindi 2 mg granules in capsules for opening
Alkindi 5 mg granules in capsules for opening
hydrocortisone

⚠ **Warning** Alkindi granules come in a capsule that must be opened before use, discard the empty capsule after use out of reach of children. Do NOT swallow the capsule – small children may choke.

Read all of this leaflet carefully before you start giving 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 your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as those of the child for whom this medicine has been prescribed.
- If your child gets 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 Alkindi is and what it is used for

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

Hydrocortisone is a synthetic version of the natural hormone cortisol. Cortisol is made by the adrenal glands in the body. Alkindi is for use in children and adolescents aged birth to 18 years when the body is not making enough cortisol, because part of the adrenal gland is not working (adrenal insufficiency, often caused by an inherited condition called congenital adrenal hyperplasia).

2. What you need to know before you give Alkindi

Do not give Alkindi:
- If your child is allergic to hydrocortisone or any of the other ingredients of this medicine (listed in section 6).

- If your child has difficulties swallowing food, or is a premature baby who cannot yet be fed by mouth.

Warnings and precautions
Talk to your endocrinologist or pharmacist before giving Alkindi:

- if your child is unwell or has an infection. The endocrinologist may need to increase the dose of Alkindi temporarily; talk to your endocrinologist if your child is unwell.

- if your child has an adrenal crisis. If your child is vomiting or seriously unwell, your child may need an injection of hydrocortisone. Your endocrinologist will train you how to do this in an emergency.

- if your child is due for a vaccination. Taking Alkindi should not stop your child being vaccinated. Let your endocrinologist know when your child is due for vaccinations.

- if your child is due for an operation. Let the anaesthetist know your child is receiving Alkindi before your child has their operation.

- if your child is being fed through a nasogastric tube. Alkindi granules are not suitable for giving through a nasogastric tube as the granules may block the tube.

- when your child is changing to Alkindi from another hydrocortisone preparation. Differences between hydrocortisone preparations when changing to Alkindi may mean your child could be at risk of receiving an incorrect dose of hydrocortisone in the first week after switching to Alkindi. This may lead to a risk of adrenal crisis. You should watch your child carefully in the week after changing to Alkindi. Your doctor will tell you when you can increase the dose of Alkindi if there are symptoms of adrenal crisis such as unusual tiredness, headache, a raised or low temperature or vomiting. If this happens medical attention should be sought right away.

You should not stop giving Alkindi without checking with your endocrinologist as this could make your child seriously unwell very quickly.

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

- Too much Alkindi can affect your child's growth, so your endocrinologist will adjust the dose depending on your child's size and monitor your child's growth carefully. Let your endocrinologist know if you are worried about your child's growth (see section 4).

- Too much Alkindi can affect your child's bones so your endocrinologist will adjust the dose depending on your child's size.

- Some adult patients taking hydrocortisone became anxious, depressed or confused. It is not known if this would happen with children, but tell your endocrinologist if your child develops any unusual behaviour after starting Alkindi (see section 4).

- In some patients with allergies to other medicines, allergy to hydrocortisone has been seen. Tell your endocrinologist straight away if your child has any reaction like swelling or shortness of breath after being given Alkindi.

- Contact your endocrinologist if your child has blurred vision or other visual disturbances.

Alkindi granules can sometimes appear in a child's nappy or poo after taking Alkindi. This is because the centre of the granule is not absorbed in the gut after it has released the medicine. This does not mean the medicine will not work and you do not need to give your child another dose.

Other medicines and Alkindi
Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines.

Some medicines can affect the way that Alkindi works, and may mean that your endocrinologist needs to alter your child's dose of Alkindi.

Your endocrinologist may need to increase your child's dose of Alkindi if your child take certain medicines, including:
- Medicines used to treat epilepsy: phenytoin, carbamazepine, and oxcarbazepine.
- Medicines used to treat infections (antibiotics): rifampicin and rifabutin.
- Medicines called barbiturates, which can be used to treat convulsions (including phenobarbital and primidone).
- Medicines used to treat AIDS: efavirenz and nevirapine.

Your endocrinologist may need to decrease your child's dose of Alkindi if your child 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.

Alkindi with food and drink
Some food and drink may affect the way Alkindi works, and may need your doctor to decrease your child's dose. These include:
- Grapefruit juice.
- Liquorice.

Pregnancy, breast-feeding and fertility
Hydrocortisone can be used during pregnancy and breast-feeding when the body is not making enough cortisol.

There is no information on any effects of Alkindi on fertility.

Driving and using machines
Alkindi has no influence on a child's ability to perform skilled tasks (e.g. riding a bicycle) or using machines.

3. How to give Alkindi

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

Your endocrinologist will decide on the right dose of Alkindi based on your child's weight or size (body surface area) and then adjust the dose of Alkindi as your child grows. During illnesses, around the time of surgery and during times of serious stress, your endocrinologist may recommend additional doses of Alkindi and may also advise that your child receives another corticosteroid instead of, or as well as, Alkindi.

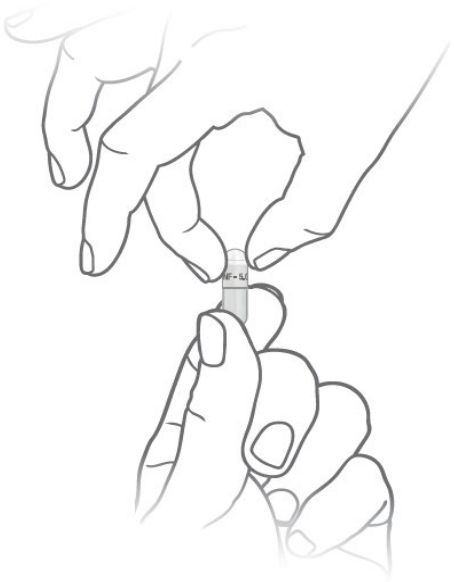
How to give this medicine
The granules should be given into the mouth and should not be chewed. The capsule shell should not be swallowed but should be carefully opened as follows:

How to open the Alkindi capsule and give the granules

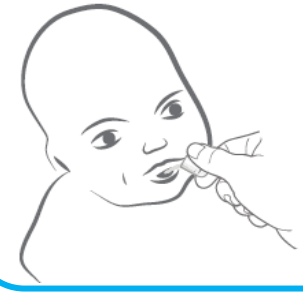
1 Hold capsule so that the text is at the top and tap the capsule to make sure the granules are at the bottom

2 Gently squeeze the bottom of the capsule

3 Twist off the top of the capsule



4 Pour all granules out of capsule



Either pour all the granules directly onto the child's tongue

OR pour all the granules directly onto a spoon and place them in the mouth

OR for children who are able to take soft food, sprinkle the granules onto a spoonful of cold or room temperature soft food (such as yoghurt or fruit puree) and give immediately

Whichever method is used, tap the capsule to ensure all the granules are removed.

If you give the granules directly into the mouth, give a drink (e.g. water, milk, breast-milk or formula-milk) immediately after administration to help ensure all granules are swallowed.

If you give the granules sprinkled onto a spoonful of soft food, administer immediately (within 5 minutes) and do not store for future use.

DO NOT add the granules to liquid before administration as this can result in less than the full dose being given, and might also dissolve the taste masking of the granules allowing the bitter taste of hydrocortisone to become apparent.

⚠ **Warning** Alkindi granules come in a capsule that must be opened before use, discard the empty capsule after use out of reach of children. Do NOT swallow the capsule – small children may choke.

If you give more Alkindi than you should
If you give your child more Alkindi than you should, contact your endocrinologist or pharmacist for further advice as soon as possible.

If you forget to give Alkindi or your child had incomplete dose
If a full dose of Alkindi is missed, give your child that dose as soon as you remember, as well as their next dose at the usual time, even if this means that your child receives two doses at the same time.

Contact your healthcare provider if your child regurgitates, vomits or spits out most of the granules in a dose administered, as a repeat dose may be required to avoid adrenal insufficiency.

If you stop giving Alkindi
Do not stop giving your child Alkindi without asking your endocrinologist first. Stopping the medicine suddenly could quickly make your child very unwell.

If your child becomes unwell
Tell your endocrinologist or pharmacist if your child becomes ill, suffers severe stress, gets injured or is about to have surgery because your endocrinologist may need to increase the dose of Alkindi in these circumstances (see section 2).

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.

The following side effects have been reported for hydrocortisone medicines used to replace cortisol:

Frequency not known (cannot be estimated from the available data):

- Changes in behaviour including:
  - loss of contact with reality (psychosis) with sensations that are not real (hallucinations) and mental confusion (delirium).
  - overexcitement and overactivity (mania).
  - intense feeling of happiness and excitement (euphoria).

  If your child has a dramatic change in behaviour, contact your endocrinologist (see section 2).

- Stomach pains (gastritis) or feeling sick (nausea).

  Contact your endocrinologist if your child complains of these.

- Changes in blood potassium levels, leading to excessive alkalinity of body tissues or fluids (hypokalaemic alkalosis).

  Your endocrinologist will monitor your child's potassium levels to check for any changes.

Long-term treatment with hydrocortisone may be associated with changes in the development of bones and reduced growth. Your endocrinologist will monitor your child's growth and bones (see section 2).

Reporting of side effects
If your child gets 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 Alkindi

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.

Do not store above 30°C. Store in the original bottle in order to protect from light.

Once the bottle has been opened, use the capsules within 60 days.

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 Alkindi contains

- The active substance is hydrocortisone
  Alkindi 0.5 mg granules in capsules for opening: each capsule contains 0.5 mg of hydrocortisone
  Alkindi 1 mg granules in capsules for opening: each capsule contains 1 mg of hydrocortisone
  Alkindi 2 mg granules in capsules for opening: each capsule contains 2 mg of hydrocortisone
  Alkindi 5 mg granules in capsules for opening: each capsule contains 5 mg of hydrocortisone
- The other ingredients are microcrystalline cellulose, hypromellose, magnesium stearate and ethyl cellulose.
- The capsule is made from hypromellose.
- The printing ink on the 0.5 mg capsules contains shellac, propylene glycol, concentrated ammonia solution, potassium hydroxide and red iron oxide (E172).
- The printing ink on the 1 mg strength capsule contains shellac, propylene glycol, concentrated ammonia solution and indigotine (E132).
- The printing ink on the 2 mg strength capsule contains shellac, propylene glycol, concentrated ammonia solution, indigotine (E132), yellow iron oxide (E172), and titanium dioxide (E171).
- The printing ink on the 5 mg strength capsule contains shellac, propylene glycol, concentrated ammonia solution, potassium hydroxide, titanium dioxide (E171), and black iron oxide (E172).

What Alkindi looks like and contents of the pack

White to off-white granules which are contained in a transparent colourless hard capsule for opening; the strength is printed on the capsule.

- Alkindi 0.5 mg granules in capsules for opening: the capsule (approx. 25.3 mm long) is printed with "INF-0.5" in red ink.
- Alkindi 1 mg granules in capsules for opening: the capsule (approx. 25.3 mm long) is printed with "INF-1.0" in blue ink.
- Alkindi 2 mg granules in capsules for opening: the capsule (approx. 25.3 mm long) is printed with "INF-2.0" in green ink.
- Alkindi 5 mg granules in capsules for opening: the capsule (approx. 25.3 mm long) is printed with "INF-5.0" in grey ink.

Alkindi comes in high density polyethylene plastic bottle.
Pack size: 1 bottle containing 50 capsules.

Marketing Authorisation Holder
Neurocrine Netherlands B.V.,
Van Heuven Goedhartlaan 935 A
1181LD Amstelveen
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Parc d'Activités Roubaix-Est
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This leaflet was last revised in

Other sources of information

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