Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

ALKINDI 0.5 mg

ALKINDI 1 mg

ALKINDI 2 mg

ALKINDI 5 mg

granules in capsule for opening

Active ingredient:
Each capsule for opening contains 0.5 mg, 1 mg, 2 mg or 5 mg of hydrocortisone, respectively.

Inactive ingredients and allergens in the medicinal product: See section 2, 'Important information about some of this medicine's ingredients' and section 6, 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult with your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

Important!

Alkindi granules are marketed in capsules.

Open the capsule, empty it and use the contents only according to the instructions in this leaflet. See section 3.

Discard the empty capsule and prevent access to it by children.

Swallowing the capsule may cause choking.

1. What is this medicine intended for?

Alkindi is intended as a replacement hormone therapy in instances of adrenal gland insufficiency in infants, children and adolescents (from birth up to 18 years of age).

Therapeutic group – the medicine belongs to the group of corticosteroids for systemic use – glucocorticoids.

Alkindi contains a substance called hydrocortisone, an alternative version of the natural hormone cortisol, which is the natural hormone released into the body by the adrenal glands. When these glands are not fully functioning, the amount of cortisol secreted is reduced. Alkindi constitutes a replacement for the natural hormone.

2. Before using this medicine

Do not use this medicine:

- if you/your child are sensitive (allergic) to the active ingredient (hydrocortisone) or to 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.

Special warnings about using this medicine

Before treatment with Alkindi, tell your doctor if:

- you or your child feel unwell or have an infection. The endocrinologist may temporarily increase the dosage of Alkindi.
- you or your child vomits or feels seriously unwell. In this instance, an injection of hydrocortisone may be necessary. The treating physician will instruct you how to do this in an emergency.
- your child is scheduled for a vaccination. Do not stop the treatment with Alkindi in the event of a vaccination. Inform the treating physician about when your child is supposed to receive a vaccination.
- you or your child are about to undergo surgery; inform the anesthetist that you or your child are taking Alkindi.
- your child is being fed through a nasogastric tube. Alkindi granules are not suitable for administering in this way because the granules may block the tube.
- 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 and give extra doses 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.

Do not stop giving your child's Alkindi without the advice of your endocrinologist, because this could make your child seriously unwell very quickly.

Since Alkindi is replacing the natural hormone that your child lacks, side effects are uncommon; however:

– a high amount of Alkindi may affect your child's growth. Therefore, your endocrinologist will adjust the dosage depending upon your child's size and will monitor your child's growth. Let your endocrinologist know if you are worried about your child's growth (see section 4).

– a high amount of Alkindi may affect your child's bones. Therefore, your endocrinologist will adjust the dosage depending upon your child's size.

– some adolescent patients taking hydrocortisone became anxious, depressed or confused. It is not known whether this may happen to children. Tell your endocrinologist if your child develops any unusual behavior after starting the treatment with Alkindi (see section 4).

– in some patients with allergies to other medicines, allergy to hydrocortisone has been observed. Tell your endocrinologist immediately if you or your child have any reaction, such as swelling or shortness of breath after you took Alkindi or gave it to your child.

– contact your endocrinologist if your child experiences blurred vision or other visual disturbances.

you may find Alkindi granules in your baby's diaper or stools. This is because the center of the granules was not absorbed in the gut after the medicine was released. **This does not mean that the medicine will not work! Do not give another dose**.

Children and adolescents

This medicine is indicated for infants, children and adolescents up to 18 years of age.

Tests and follow-up

A high dosage of Alkindi may affect your child's growth or bones. Therefore, during the period of treatment with the medicinal product, the endocrinologist will adjust the dosage to your child's size and will monitor your child's growth.

The endocrinologist will monitor your/your child's potassium levels.

Drug interactions

If you or your child are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Some medicines may affect the way that Alkindi works. Therefore, your endocrinologist may need to adjust the dosage of the medicine.

If one of the following medicines is being taken, an increase in the dosage of Alkindi may be required:

- medicines to treat epilepsy: phenytoin, carbamazepine and oxcarbazepine
- medicines to treat infections (antibiotics): rifampicin and rifabutin
- medicines from the family of barbiturates that are given to treat convulsions, including phenobarbital and primidone
- medicines to treat AIDS: efavirenz and nevirapine.

If one of the following medicines is being taken, a decrease in the dosage of Alkindi may be required:

- medicines to treat fungal infections: itraconazole, posaconazole and voriconazole
- medicines to treat infections (antibiotics): erythromycin and clarithromycin
- medicines to treat HIV infections and AIDS: ritonavir.

Using this medicine and food

Some foods and beverages may affect the way that the medicine works, and may require a decrease in the dosage. For example:

- grapefruit juice
- licorice.

Pregnancy, breastfeeding and fertility

Alkindi may be taken during pregnancy or breastfeeding when your body is not producing enough cortisol.

There is no information about the effects of Alkindi on fertility.

Driving and using machines

Alkindi has no influence on a child's ability to perform special tasks (such as riding a bicycle), or on the ability to operate machines.

3. How to use this medicine?

Always use a medicinal product according to your doctor's instructions.

Check with your doctor or pharmacist if you are not sure about the dosage or treatment regimen of a medicinal product.

Only the endocrinologist will determine the dosage and treatment regimen, which will be based on your/your child's weight or body surface and will be adjusted according to your/your child's growth. During situations of illnesses, surgical procedures or during episodes of extreme stress, the doctor may instruct that additional doses of Alkindi or another corticosteroid be given instead of, or in addition to, Alkindi.

Do not exceed the recommended dose.

How to take the medicine

Do not swallow the capsule whole and do not chew the capsule!

Warning! Alkindi granules are marketed in capsules that must be opened before use. Discard the empty capsule after use and keep it out of the reach of children. The capsule must not be swallowed – small children may choke.

Hold the capsule so that the writing is at the top; tap lightly on the capsule to make sure that the granules are at the bottom; gently squeeze the bottom part of the capsule; twist off the upper part of the capsule (see illustrations 1 – 3 at the end of this leaflet).

Open and empty the entire contents of the capsule (the granules) and take them in one of the following ways (see illustration 4 at the end of this leaflet):

- empty the granules on the tongue and immediately drink a beverage, such as water, milk; for infants: breast-milk or formula.
- empty the granules onto a spoonful of cold or room-temperature soft food, such as yogurt or fruit puree and swallow immediately (within 5 minutes). Do not store for later use.
- empty the granules onto a spoon and put in the mouth.

Do not add the granules to a liquid before taking them because this may reduce the amount of medicine that you take and may dissolve the ingredient that masks the taste of the medicine, resulting in a bitter taste.

Whichever method you use, tap the capsule to make sure that all of the granules are emptied from the capsule.

If you have accidentally taken or given your child a higher dose, contact the treating physician or a pharmacist without delay.

If you forget to take the medicine or to give your child a dose at the scheduled time, take the dose as soon as you remember and take the next dose at the usual time.

Adhere to the treatment as recommended by your doctor.

If you stop giving this medicine to your child or stop taking this medicine without consulting with your doctor, **this may cause you or your child to feel seriously unwell (**adrenal crisis**).**

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult with your doctor or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using Alkindi may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Refer to a doctor immediately if:

Reactions such as shortness of breath or swelling have been observed; these may be indications of an allergic reaction (see section 2).

The following side effects have been reported for hydrocortisone medicines used for cortisol hormone replacement therapy:

Unknown frequency (cannot be estimated from the available data):

Refer to the treating endocrinologist if any of the following appear:

- severe changes in behavior, including:
  - loss of touch with reality (psychosis) accompanied by feelings that are not real (hallucinations) and severe confusion (delirium)
  - overenthusiasm or hyperactivity (mania)
  - intense feelings of happiness and excitement (euphoria)
- Pain in upper abdomen – stomach (gastritis)
- Nausea
- Changes in the level of potassium in the blood, causing excessive alkalinity of body tissues or fluids (hypokalaemic alkalosis).

In children, it has been found that prolonged treatment with hydrocortisone may affect bone development and retard growth – the doctor will monitor the child's growth and bones (see section 2).

If any side effect appears, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult with your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il.

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:

Store below 30°C.

Store in the original package to protect from light.

Once the bottle has been opened, store below 30°C in the original package to protect from light and use within 60 days.

6. Additional information

In addition to the active ingredient, this medicine also contains:
microcrystalline cellulose, hypromellose, ethyl cellulose, magnesium stearate.

The capsule is made of hypromellose. The printing ink on the capsules contains, according to the strength of the medicine:
0.5 mg (red): shellac, propylene glycol, concentrated ammonia solution, red iron oxide (E172), potassium hydroxide
1 mg (blue): shellac, propylene glycol, concentrated ammonia solution, indigotine (E132)
2 mg (green): shellac, propylene glycol, concentrated ammonia solution, indigotine (E132), yellow iron oxide (E172), titanium dioxide (E171)
5 mg (grey): shellac, propylene glycol, concentrated ammonia solution, titanium dioxide (E171), black iron oxide (E172), potassium hydroxide

What the medicine looks like and contents of the pack

Alkindi is packed in a white bottle and is packaged in a carton.

The medicine is provided as white or off-white granules inside a transparent, colorless capsule **for opening (not for swallowing!)** with the strength printed in colored ink on the capsule:

Alkindi 0.5 mg – the capsule, approx. 25.3 mm long, is printed with “INF-0.5” in red ink

Alkindi 1 mg – the capsule, approx. 25.3 mm long, is printed with “INF-1.0” in blue ink

Alkindi 2 mg – the capsule, approx. 25.3 mm long, is printed with “INF-2.0” in green ink

Alkindi 5 mg – the capsule, approx. 25.3 mm long, is printed with “INF-5.0” in grey ink.

Each bottle contains 50 capsules for opening, and a desiccant. Do not remove the desiccant from the bottle.

Registration holder’s name and address: Medomie Pharma Ltd., 5358305, POB 816, Givatayim.

Manufacturer’s name and address:
Diurnal Europe B.V.,
Van Heuven Goedhartlaan 935 A,
1181LD Amstelveen,
The Netherlands.

Revised in March 2024

Registration number of the medicine in the Ministry of Health’s National Drug Registry:

Alkindi 0.5 mg – 164-46-35964-00

Alkindi 1 mg – 164-47-35965-00

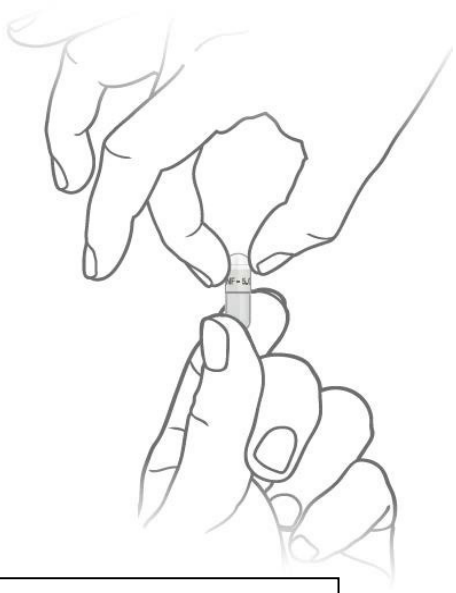
Alkindi 2 mg – 164-48-35966-00

Alkindi 5 mg – 164-49-35967-00

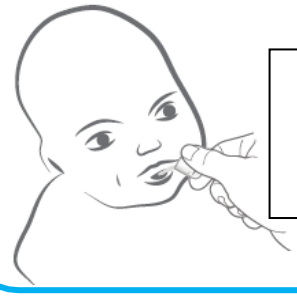
1. Hold the capsule with the writing at the top and tap lightly on the capsule to make sure that the granules are at the bottom

2. Gently squeeze on the bottom part of the capsule

3. Twist off the bottom part of the capsule



4. Pour all of the granules out of the capsule



directly onto your child's tongue

or pour all of the granules into a spoon and put them in the mouth

or, if your child is able to swallow soft food, sprinkle the granules onto a spoonful of cold or room-temperature soft food (such as yogurt or fruit puree) and give immediately.

Whichever method is used, tap the capsule to make sure that all of the granules are emptied from the capsule.

If you are giving the granules directly into the mouth, give your child a drink (water, milk, breast-milk or breast-milk substitute) immediately afterwards in order to make sure that your child has swallowed all of the granules.

If you give the granules sprinkled onto a spoonful of soft food, give the medicine immediately (within 5 minutes). Do not save the granules for later use.

Do not add the granules to a liquid **before taking** it. This may cause you to give less than the required dose, and the coating on the granules that masks the taste of hydrocortisone may dissolve and a bitter taste will be tasted.