Risk of acute adrenal insufficiency when switching from crushed or compounded oral hydrocortisone formulations to Alkindi (hydrocortisone granules in capsules for opening)

Dear Healthcare professional,

Diurnal Europe B.V. in agreement with the European Medicines Agency and the <National Competent Authority > would like to inform you of the following:

Summary

- **Adrenal crisis has been reported in an infant who was switched from hydrocortisone soluble tablets to Alkindi (hydrocortisone granules in capsules for opening).**
- **Acute adrenal insufficiency can occur when switching to Alkindi granules due to a potential risk of inaccurate dosing possible with other oral hydrocortisone formulations, crushed or compounded.**
- **To prevent adrenal crisis after switching to Alkindi granules, carers should be advised to carefully observe the child during the first week for symptoms of adrenal insufficiency such as tiredness, headache, unstable temperature and vomiting.**
- **Carers should be advised to give extra doses of Alkindi granules as recommended in the product information, if the child develops symptoms of adrenal insufficiency and seek immediate medical attention.**

Background on the safety concern

Alkindi hydrocortisone granules in capsules for opening are indicated for replacement therapy of adrenal insufficiency in infants, children and adolescents (from birth to < 18 years old).

A case has been reported of an infant developing severe adrenal insufficiency when switched from hydrocortisone soluble tablets to Alkindi granules. The child experienced an adrenal crisis approximately 48 hours after starting Alkindi. The child had no predisposition to adrenal crisis and there was no indication that Alkindi had been administered incorrectly, nor any symptoms of malabsorption.

Due to the insolubility of hydrocortisone, not preparing hydrocortisone soluble tablets in accordance with manufacturer's instructions may risk variable dosing and make conversion to other forms of hydrocortisone in the youngest children difficult. Similarly, variable dosing may result from the use of crushed or compounded hydrocortisone formulations in the youngest children.

When converting children from conventional oral hydrocortisone formulations, crushed or compounded, to Alkindi granules, especially in the youngest children least able to communicate adrenal insufficiency symptoms, the carers should be advised to observe the child carefully and be

instructed to give the child extra doses of Alkindi if the child develops any symptoms of adrenal insufficiency such as tiredness, headache, temperature instability or vomiting, in accordance with the recommendations in the product information. In addition, the carers and patients should be advised to seek medical advice if such symptoms occur.

Close clinical monitoring of patients is recommended in the first week after switch. If a child requires additional dosing during the first week after transferring from conventional oral hydrocortisone formulations, crushed or compounded, to Alkindi hydrocortisone granules in capsules for opening, an increase in the daily dose of Alkindi should be considered.

The product information for Alkindi will be updated to reflect this new information.

Call for reporting

Healthcare professionals should report any suspected adverse reactions associated with the use of Alkindi in accordance with the national spontaneous reporting system <*include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system*>.

Company contact point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address (company contact point in the concerned EU MS should be included, respectively)>

Yours Faithfully

Medical Director Diurnal Europe BV.

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Alkindi (hydrocortisone granules in capsules for opening)/ Hydrocortisone
Marketing authorisation holder(s)	Diurnal Europe BV.
Safety concern and purpose of the communication	Risk of acute adrenal insufficiency when switching from oral hydrocortisone formulations, crushed or compounded, to Alkindi
DHPC recipients	Paediatric and adult endocrinologists. The target group should be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU member states where Alkindi is marketed.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	14/01/2021
DHPC and communication plan (in English) agreed by CHMP	18/01/2021
Submission of translated DHPCs to the national competent authorities for review	25/01/2021
Agreement of translations by national competent authorities	27/01/2021
Dissemination of DHPC	04/02/2021