Diurnal Europe B.V.
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The Netherlands

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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 Medicines and Healthcare Products Regulatory Agency (MHRA) 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 could 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 evidence of acute illness and there was no indication that Alkindi had been administered incorrectly, nor any symptoms of malabsorption.

Due to the insolubility of hydrocortisone, preparing hydrocortisone soluble tablets not in accordance with the manufacturer's instructions may risk variable dosing and make conversion to other forms of

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hydrocortisone in younger 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, including 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 immediate 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, including 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
Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

You can report via:

- the Yellow Card website https://yellowcard.mhra.gov.uk/
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours. When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Adverse events should also be reported to Diurnal using the following contact details;
email adverse-events@diurnal.co.uk or telephone +44 (0) 7917 334899.

Further information can be obtained from info@diurnal.co.uk

Company contact point

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Yours Faithfully

Dr. John Porter

Medical Director Diurnal Europe BV.

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