

FERRING

PHARMACEUTICALS

Dear Doctor,

IMPORTANT SAFETY INFORMATION

Desmopressin Nasal Spray: Removal of the Primary Nocturnal Enuresis Indication

At the request of the MHRA, the indication for the treatment of primary nocturnal enuresis (PNE) has been removed from all desmopressin nasal spray products, including Desmospray, which is marketed by Ferring Pharmaceuticals Limited. Desmospray remains available for the treatment of patients with cranial diabetes insipidus or nocturia associated with multiple sclerosis. In comparison with oral formulations of desmopressin, nasal forms were associated with the majority of serious adverse drug reactions (ADRs) reported in patients with PNE. Rare, serious ADRs included hyponatraemia, water intoxication and convulsions. As the risk benefit profile of the oral formulations is more favourable than the nasal spray, the nasal form should no longer be used for the treatment of PNE in adults and children.

Prescribing Advice

Patients may complete their current course of treatment with desmopressin nasal spray. At their next routine review, patients needing continued treatment should only be prescribed an oral form of desmopressin. Regardless of the dose of spray they have been taking, all patients starting treatment with oral desmopressin should start at the lower recommended dose, which should only be increased if necessary to achieve control of symptoms. Prescribers should also be aware that there is a possible risk of severe hyponatraemia when a nasal desmopressin formulation is used to treat patients with cranial diabetes insipidus.

Further Information

Desmopressin is a synthetic analogue of vasopressin with increased antidiuretic activity and a prolonged duration of action in comparison with the natural peptide. The nasal spray has greater bioavailability than the oral formulation. Both forms produce a sustained decrease in urine output and a decrease in plasma osmolality which can result in hyponatraemia and water intoxication in the presence of an inappropriate fluid intake. Hyponatraemia is a rare but serious ADR, which has been reported at a rate of approximately 15 cases per 100,000 patient years of exposure for nasal formulations and 6 cases per 100,000 patient years for oral formulations, and has been predominantly associated with overdose, excessive fluid intake or



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inappropriate use. It is not known whether these adverse effects are dose-related but there is strong evidence of a relationship to the formulation. Since the majority of cases of hyponatraemia occurred with the nasal formulation in the PNE indication, only oral formulations should be used in PNE. The risk of hyponatraemia occurring with oral desmopressin can be further reduced by closely following the advice in the Summary of Product Characteristics (SPC) and the Patient Information Leaflet (PIL).

Further information can be found on the MHRA website: www.mhra.gov.uk

Changes to the Summary of Product Characteristics (SPC)

Section 4.1 Therapeutic Indications

Remove: 'The treatment of primary nocturnal enuresis'

Section 4.4 Special Warnings and Precautions for Use

Add: 'There is some evidence from post-marketing data for the occurrence of severe hyponatraemia in association with the nasal spray formulation of desmopressin, when it is used in the treatment of cranial diabetes insipidus.'

There are also further consequential changes to sections 4.2, 4.3, 4.5 and 4.8. The updated SPCs and PILs are available at www.emc.medicines.org.uk

Reporting of suspected adverse events

Please report any cases of suspected adverse reactions in association with the use of desmopressin to the MHRA at www.yellowcard.gov.uk.

Communication information

If you have any enquiries or need additional information, please contact the Medical Information Department at Ferring Pharmaceuticals Limited by telephone or by email at medical@ferring.com. The following telephone number is available for provision of medical information during normal working hours and for out of hours medical emergencies: 01753 214800.

Yours sincerely,



A D Waters

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