

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-333**

**PHARMACOLOGY REVIEW**

**REVIEW AND EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA:**

**Key Words:** arginine vasopressin

**Reviewer:** Karen L. Davis-Bruno, Ph.D.; Supervisory Pharmacologist

**Division of Metabolic and Endocrine Drug Products; HFD-510**

**Review Completion:**

**Review #1**

**Submission Date:** 11/7/00

**NDA 21-333**

**Information to the Sponsor:** No

**Sponsor:** Ferring Pharmaceuticals, Tarrytown, NY

**Manufacturer:** Ferring Pharmaceuticals, Sweden

**DRUG:** Minirin Nasal Spray

**Generic name:** desmopressin acetate—a synthetic structural analogue of arginine vasopressin. The differences between desmopressin acetate and arginine vasopressin is that the amino group is removed from the N-terminus and L-arginine in position 8 is replaced by D-arginine. These changes are reported to increase the antidiuretic activity from 400 IU/mg to 4000 IU/mg while reducing the vasopressor effect from 400 IU/mg to 0.27 IU/mg.

**Relevant NDAs:** 17-922, DMF ———, NDA 18-938 (injection)

**Drug Class:** anti-diuretic

**Indication:** diabetes insipidus, primary nocturnal enuresis

**Clinical Formulation:** 0.01% solution where the compression pump delivers 0.1 ml/spray containing 10 mcg desmopressin acetate equivalent to 40 IU.

**Excipients:** each ml of product (5 ml total) contains 0.1 mg desmopressin acetate, 5 mg chlorobutanol, 9 mg sodium chloride and HCl to adjust pH ~4

**Route of Administration:** intranasal

**Previous Clinical Experience:** extensive see approved NDAs

**Introduction and Drug History:** An identical product was manufactured by the sponsor and is approved but not marketed under NDA 17-922 for diabetes insipidus. A supplemental application for primary nocturnal enuresis was approved 11/28/89. The NDA is currently owned by Aventis Pharmaceuticals Inc. a letter of authorization to reference the NDA/DMF is provided. The desmopressin acetate nasal spray was reformulated from a refrigerated to a room temperature preparation. Aventis markets the room temperature desmopressin acetate nasal spray which is manufactured by Ferring under NDA 17-922. The current NDA application is for the refrigerated formulation of desmopressin acetate nasal spray.

Studies Reviewed within this Submission: NDA 17-922 is cross referenced for preclinical data.

**OVERALL SUMMARY AND EVALUATION:**

Safety Evaluation: There are no preclinical safety issues with this product.

Conclusions: Pharmacology recommends approval.

**COMMUNICATIONS REVIEW:**

Labeling Review: Two changes are proposed compared to the approved labeling under NDA 17-922 for Desmopressin Acetate Nasal Spray (Aventis). These changes include a name change of the drug product to Minirin Nasal Spray and a change in the sponsor from Aventis to Ferring Pharmaceuticals who is also the manufacturer for both products. The draft labeling is adequate as proposed for the pharmacology sections.

RECOMMENDATIONS: none

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Karen Davis-Bruno; Ph.D.  
Supervisory Pharmacologist, DMEDP

Cc:HFD510/Davis-Bruno/McCort

/s/

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Karen Davis-Bruno

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PHARMACOLOGIST

P/T review for NDA 21-333 recommends approval, no labelling changes

P/T review