

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin
Mannitol
Citric acid, anhydrous

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store in the original package.

6.5 Nature and contents of container

PVC/Polyamide/Aluminium/Polyamide/PVC blisters. Top foil consists of Paper/Polyester terephthalate/Aluminium/heat seal lacquer. Strips of 10 oral lyophilisates in packs of 30 oral lyophilisates.

6.6 Instructions for use and handling

None.

7. MARKETING AUTHORISATION HOLDER

Ferring Pharmaceuticals Ltd.
The Courtyard
Waterside Drive
Langley
Berkshire SL3 6EZ
United Kingdom.

8. MARKETING AUTHORISATION NUMBER

DesmoMelt 120 micrograms oral lyophilisate PL 03194/0094
DesmoMelt 240 micrograms oral lyophilisate PL 03194/0095

9. DATE OF FIRST AUTHORISATION

19th January 2006

10. DATE OF REVISION OF THE TEXT

November 2006

11. LEGAL CATEGORY

POM

*DesmoMelt is a trademark of Ferring BV.

FERRING

PHARMACEUTICALS

DesmoMelt* 120 & 240 micrograms
oral lyophilisate

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

DesmoMelt 120 micrograms oral lyophilisate
DesmoMelt 240 micrograms oral lyophilisate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each unit contains 120 or 240 micrograms desmopressin (as acetate).

For excipients, see 6.1

3. PHARMACEUTICAL FORM

Oral lyophilisate.

DesmoMelt 120 micrograms oral lyophilisate
White, round, oral lyophilisate marked with two drop shaped figures on one side.

DesmoMelt 240 micrograms oral lyophilisate
White, round, oral lyophilisate marked with three drop shaped figures on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DesmoMelt is indicated for the treatment of primary nocturnal enuresis.

4.2 Posology and method of administration

DesmoMelt is for sublingual use.

Children (from 5 years of age) and adults (up to 65 years of age) with normal urine concentrating ability who have primary nocturnal enuresis should take 120 micrograms at bedtime administered sublingually and only if needed should the dose be increased to 240 micrograms sublingually.

The need for continued treatment should be reassessed after 3 months by means of a period of at least 1 week without DesmoMelt.

4.3 Contraindications

DesmoMelt is contraindicated in cases of cardiac insufficiency and other conditions requiring treatment with diuretic agents. DesmoMelt should only be used in patients with normal blood pressure.

Before prescribing DesmoMelt, the diagnoses of psychogenic polydipsia and alcohol abuse should be excluded.

Desmopressin should not be prescribed to patients over the age of 65 for the treatment of primary nocturnal enuresis.

4.4 Special warnings and precautions for use

Care should be taken with patients who have reduced renal function and/or cardiovascular disease or cystic fibrosis. In chronic renal disease the antidiuretic effect of DesmoMelt would be less than normal.

When DesmoMelt is used for the treatment of enuresis, fluid intake must be limited from 1 hour before until 8 hours after administration.

Patients being treated for primary nocturnal enuresis should be warned to avoid ingesting water while swimming and to discontinue DesmoMelt during an episode of vomiting and/or diarrhoea until their fluid balance is once again normal.

Precautions to prevent fluid overload must be taken in:

- conditions characterised by fluid and/or electrolyte imbalance
- patients at risk for increased intracranial pressure.

4.5 Interactions with other medicinal products and other forms of interaction

Substances which are known to induce SIADH e.g. tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect leading to an increased risk of water retention and/or hyponatraemia.

NSAIDs may induce water retention and/or hyponatraemia.

Concomitant treatment with loperamide may result in a 3-fold increase of desmopressin plasma concentrations, which may lead to an increased risk of water retention and/or hyponatraemia. Although not investigated, other drugs slowing intestinal transport might have the same effect.

A standardised 27% fat meal significantly decreased the absorption (rate and extent) of a 0.4mg dose of oral desmopressin tablets. Although it did not significantly affect the pharmacodynamic effect (urine production and osmolality) there is the potential for this to occur at lower doses. If a diminution of effect is noted, then the effect of food should be considered before increasing the dose.

4.6 Pregnancy and lactation

Pregnancy:

Data on a limited number (n=53) of exposed pregnancies in women with diabetes insipidus indicate rare cases of malformations in children treated during pregnancy. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development.

Caution should be exercised when prescribing to pregnant women. Blood pressure monitoring is recommended due to the increased risk of pre-eclampsia.

Lactation:

Results from analyses of milk from nursing mothers receiving high dose desmopressin (300 micrograms intranasally) indicate that the amounts of desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Side-effects include headache, stomach pain and nausea. Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported. Very rare cases of emotional disturbances in children have been reported. Treatment with desmopressin without concomitant reduction of fluid intake may lead to water retention/hyponatraemia with

accompanying symptoms of headache, nausea, vomiting, weight gain, decreased serum sodium and in serious cases, convulsions.

4.9 Overdose

An overdose of DesmoMelt leads to a prolonged duration of action with an increased risk of water retention and/or hyponatraemia.

Treatment:

Although the treatment of hyponatraemia should be individualised, the following general recommendations can be given. Hyponatraemia is treated by discontinuing the desmopressin treatment, fluid restriction and symptomatic treatment if needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vasopressin and analogues
ATC code: H01B A02

In its main biological effects, desmopressin does not differ qualitatively from vasopressin. However, desmopressin is characterised by a high antidiuretic activity whereas the uterotonic and vasopressor actions are extremely low.

5.2 Pharmacokinetic properties

The overall mean systemic bioavailability of desmopressin administered sublingually as Melts at doses of 200, 400 and 800 micrograms is 0.25% with a 95% confidence interval of 0.21% - 0.31%. The C_{max} was 14, 30 and 65pg/ml after administration of 200, 400 and 800 micrograms respectively. t_{max} was observed at 0.5 – 2.0 hours after dosing. The geometric mean terminal half-life is 2.8 (CV = 24%) hours.

Correlation table between desmopressin in Tablet and Melt forms:

| Tablet | Tablet | Melt | Melt |
|----------------------|------------------------|------------------------|-------------------------------------|
| Desmopressin acetate | Desmopressin free base | Desmopressin free base | Desmopressin acetate |
| 0.1mg | 89 micrograms | 60 micrograms | Approx. 67 micrograms ⁺ |
| 0.2mg | 178 micrograms | 120 micrograms | Approx. 135 micrograms ⁺ |
| 0.4mg | 356 micrograms | 240 micrograms | Approx. 270 micrograms ⁺ |

⁺calculated for comparative purposes

The distribution volume of desmopressin after intravenous administration is 33 L (0.41 L/kg). Desmopressin does not cross the blood-brain barrier. Desmopressin exhibits a moderate to high variability in bioavailability, both within and between subjects. Concomitant use of food decreases the rate and extent of absorption by 40%.

In vitro, in human liver microsome preparations, it has been shown that no significant amount of desmopressin is metabolised in the liver and thus human liver metabolism *in vivo* is not likely to occur.

It is unlikely that desmopressin will interact with drugs affecting hepatic metabolism, since desmopressin has been shown not to undergo significant liver metabolism in *in vitro* studies with human microsomes. However, formal *in vivo* interaction studies have not been performed.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.