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Desmopressin Oral Lyophilisate

General Notices

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Biological and Biotechnological Products
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Target Publication Date (subject to change)	BP 2026
Notes:	Revised monograph Updated to more accurately reflect the salt form of the licensed preparations

Action and use

Vasopressin analogue; treatment of diabetes insipidus.

DEFINITION

Desmopressin Oral Lyophilisate contains Desmopressin Acetate with suitable excipients.

The oral lyophilisate complies with the requirements stated under Tablets and with the following requirements.

Content of desmopressin acetate, $C_{48}H_{68}N_{14}O_{14}S_2$

90.0 to 110.0% of the stated amount of the peptide.

IDENTIFICATION

In the Assay, the principal peak in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions and the *normalisation procedure*.

(1) Shake a quantity of the oral lyophilisate with 10 mL of a mixture of 50% of the buffer solution and 50% of *water* to produce a solution containing 0.0025% w/v of the peptide.
(2) Dissolve the contents of a vial of *desmopressin impurity standard BPCRS* in 4 mL of a mixture of 50% of the buffer solution and 50% of *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 3.0 mm) packed with nitrile groups chemically bonded to porous silica particles (5 µm) (Zorbax-SB-CN is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 0.6 mL per minute.
(d) Use a column temperature of 50°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 200 µL of each solution.

Buffer solution

0.05 M ammonium acetate buffer solution, pH 4.6, if necessary adjusted with acetic acid.

Mobile phase A

15 volumes of *acetonitrile*, 35 volumes of *water* and 50 volumes of the Buffer solution.

Mobile phase B

15 volumes of *water*, 40 volumes of *acetonitrile* and 45 volumes of the Buffer solution.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-16	100	0	isocratic
16-31	100→0	0→100	linear gradient
31-36	0	100	isocratic
36-37	0→100	100→0	linear gradient
37-41	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions the retention time for the first peak: in solution (2) is about 9 minutes and about 11 minutes for desmopressin.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (2), the *resolution* between the two principal peaks is at least 2.0;

the peak due to desmopressin is clearly separated from any peaks due to excipients stated on the label.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not more than 2.0%;

the total area of any such peaks is not more than 4.0%.

Disregard any peak due to the solvent, any excipients stated on the label and any peak with an area less than 0.05%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a suitable quantity of the oral lyophilisate with 10 mLof a mixture of 50% of the Buffer solution and 50% of *water*, to give a final concentration of 0.0025% w/v of the peptide.
(2) Dissolve the contents of a vial of *desmopressin BPCRS* in a mixture of 50% of the Buffer solution and 50% of *water*. to give a final concentration of 0.0025% w/v of the peptide.
(3) Dissolve the contents of a vial of *desmopressin impurity standard BPCRS* in 4 mL of a mixture of 50% of the Buffer solution and 50% of *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 3.0 mm) packed with nitrile groups chemically bonded to porous silica particles (5 µm) (Zorbax-SB-CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.6 mL per minute.
(d) Use a column temperature of 50°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 200 µL of each solution.

Carry out isocratic elution for at least 16 minutes for each run.

MOBILE PHASE

Buffer solution 0.05M ammonium acetate buffer solution, pH 4.6, 15 volumes of *acetonitrile*, 35 volumes of *water* and 50 volumes of the Buffer solution.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the two principal peaks and desmopressin is at least 2.0;

the peak due to desmopressin is clearly separated from any peaks due to excipients stated on the label.

DETERMINATION OF CONTENT

Calculate the content of $C_{48}H_{68}N_{14}O_{14}S_2$ in each tablet from the chromatograms obtained and from the declared content of $C_{46}H_{64}N_{14}O_{12}S_2$ in *desmopressin BPCRS*.

STORAGE

Desmopressin Oral Lyophilisate should be protected from light and moisture.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Desmopressin.