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Domperidone Tablets

General Notices

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

EAG/Panel/Working Party	Medicinal Chemicals 1
Contact Details	graziella.li-ship@mhra.gov.uk jonathan.campbell@mhra.gov.uk
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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Dissolution** limit updated to Q value, sample time reduced **Impurities** section added

Action and use

Peripheral dopamine receptor antagonist; antiemetic.

DEFINITION

Domperidone Tablets contain Domperidone Maleate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of domperidone, $C_{22}H_{24}ClN_5O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in a mixture of equal volumes of *dichloromethane* and *methanol*.
(1) Shake a quantity of the powdered tablets containing the equivalent of 10 mg of domperidone with 10 mL of solvent and filter through a glass microfibre filter (a Whatman GF/C is suitable).
(2) 0.127% w/v of *domperidone maleate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a precoated *silica gel F_{254}* plate (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*. Spray the plate with *potassium iodobismuthate solution* and examine again.

MOBILE PHASE

5 volumes of a solution prepared by dissolving 1.36 g of *sodium acetate* in 50 mL of *water*, adjusting the pH to 4.7 with *dilute acetic acid* and adding sufficient *water* to produce 100 mL, 18 volumes of *methanol*, 23 volumes of *dichloromethane* and 54 volumes of *ethyl acetate*.

CONFIRMATION

Using each method of visualisation, the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution expected to contain the equivalent of 0.001% w/v of domperidone at the maximum at 284 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.0013% w/v solution of *domperidone maleate BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of domperidone, $C_{22}H_{24}ClN_5O_2$, in the medium from the absorbances obtained and using the declared content of $C_{26}H_{28}ClN_5O_6$, in *domperidone maleate BPCRS*.

LIMITS

The amount of domperidone released is not less than 80% (Q) of the stated amount.

Related substances

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

Solution A 1 volume of 0.01M *hydrochloric acid* and 1 volume of *methanol*.

(1) To a quantity of the powdered tablets containing the equivalent of 50 mg of domperidone add 10 mL of a mixture of solution A, mix with the aid of ultrasound and filter (a 0.7-µm GMF syringe filter is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A. Dilute 1 volume of this solution to 10 volumes with the same solvent.
(3) 0.004% w/v of *domperidone impurity mixture EPCRS* (containing impurities A and D).
(4) 0.01% w/v of *domperidone maleate BPCRS* and 0.015% w/v of *droperidol BPCRS* in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Phenomenex Luna C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 280 nm.
(f) Inject 10 µL of each solution. Inject a mixture of equal volumes of 0.01M *hydrochloric acid* and *methanol* as a blank prior to the solutions.

MOBILE PHASE

Mobile phase A 0.5% w/v solution of *ammonium acetate*.

Mobile phase B *methanol*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-10	70→0	30→100	linear gradient
10-12	0	100	isocratic
12-14	0→70	100→30	linear gradient
14-24	70	30	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (4), the *resolution* between the peaks due to domperidone and droperidol is at least 2;

in the chromatogram obtained with solution (2), the *signal-to-noise ratio* of the peak due to impurity A is at least 7.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of domperidone in solution (2).

For the reporting threshold, use the concentration of domperidone in solution (2).

For peak identification, use solution (3).

Domperidone retention time: about 7 minutes.

Relative retention: impurity A, about 0.4, droperidol, about 1.04 and impurity D+E, about 1.2.

Correction factors: impurity A, multiply by 1.3.

LIMITS

— sum of impurity D and E: not more than 0.25%.

— unspecified impurities: for each impurity, not more than 0.10%.

— total impurities: not more than 0.5%.

— reporting threshold: 0.1%; disregard the peak due to maleic acid.

ASSAY

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

(1) Add sufficient *methanol* to 10 whole tablets to produce a solution containing 0.02% w/v of domperidone, mix with the aid of ultrasound and filter (a Whatman GF/C filter is suitable). To 50 mL of the filtrate add 1 mL of 0.1M *hydrochloric acid* and sufficient *water* to produce 100 mL.
(2) 0.0127% w/v of *domperidone maleate BPCRS* in a mixture of equal volumes of 0.002M *hydrochloric acid* and *methanol*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{22}H_{24}ClN_5O_2$ in the tablets using the declared content of $C_{26}H_{28}ClN_5O_6$ in *domperidone maleate BPCRS*.

STORAGE

Domperidone Tablets should be stored in an airtight container.

LABELLING

The quantity of the active ingredient is stated in terms of the equivalent amount of domperidone.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A and D+E listed under Domperidone.