Edition: BP 2025 (Ph. Eur. 11.6 update)

Melphalan Tablets

General Notices

Action and use

Cytotoxic alkylating agent.

DEFINITION

Melphalan Tablets contain Melphalan. They are coated.

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

Content of melphalan, $C_{13}H_{18}Cl_2N_2O_2$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Extract a quantity of the powdered tablets containing 25 mg of Melphalan with 50 mL of hot *methanol*, filter and dilute 5 mL of the filtrate to 500 mL with *methanol*. The *light absorption* of the resulting solution, Appendix II B, exhibits a maximum at 260 nm and a less well-defined maximum at 301 nm.
B. To the remainder of the filtrate obtained in test A add 1 mL of a 5% w/v solution of *4-(4-nitrobenzyl)pyridine* in *acetone* and evaporate to dryness. Dissolve the residue in 1 mL of hot *methanol* and add 0.1 mL of 13.5M *ammonia*. A red colour is produced.

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with 0.1M *hydrochloric acid* if necessary, expected to contain about 0.0002% w/v of Melphalan.
(2) Dilute a suitable volume of a 0.10% w/v solution of *melphalan BPCRS* in a mixture of 4 volumes of *acetonitrile* and 1 volume of 0.1M *hydrochloric acid* with sufficient 0.1M *hydrochloric acid* to produce a solution containing 0.0002% w/v.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Spherisorb ODS 1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

2.7 volumes of *glacial acetic acid*, 180 volumes of *methanol* and 200 volumes of a 0.375% w/v solution of *ammonium carbonate*.

DETERMINATION OF CONTENT

Calculate the content of melphalan, $C_{13}H_{18}Cl_2N_2O_2$ in the medium using the declared content of $C_{13}H_{18}Cl_2N_2O_2$ in *melphalan BPCRS*.

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Melphalan comply with the requirements stated under Tablets using the following method of analysis.

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

(1) 0.01% w/v of *melphalan BPCRS* in a mixture of 4 volumes of *acetonitrile* and 1 volume of 0.1M *hydrochloric acid*.
(2) Add 20 mL of a mixture of 4 volumes of *acetonitrile* and 1 volume of 0.1M *hydrochloric acid* to one tablet, mix with the aid of ultrasound for 10 minutes or until the tablet has disintegrated, filter, discarding the first 5 mL of filtrate, and use the filtrate.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Spherisorb ODS 1 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

2.7 volumes of *glacial acetic acid*, 180 volumes of *methanol* and 200 volumes of a 0.375% w/v solution of *ammonium carbonate*.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{18}Cl_2N_2O_2$ in each tablet using the declared content of $C_{13}H_{18}Cl_2N_2O_2$ in *melphalan BPCRS*.

ASSAY

For tablets containing less than 2 mg and/or less than 2% w/w of Melphalan

Use the average of the 10 individual results determined in the test for Uniformity of content.

For tablets containing 2 mg or more and 2% w/w or more of Melphalan

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

(1) 0.01% w/v of *melphalan BPCRS* in a mixture of 4 volumes of *acetonitrile* and 1 volume of 0.1M *hydrochloric acid*.

(2) Add about 300 mL of a mixture of 4 volumes of *acetonitrile* and 1 volume of 0.1M *hydrochloric acid* to 10 tablets, shake until the tablets have disintegrated (about 30 minutes), mix with the aid of ultrasound for 5 minutes, dilute to 500 mL with the same solvent mixture, filter, discarding the first 20 mL of filtrate, and use the filtrate.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Uniformity of content may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{18}Cl_2N_2O_2$ in the tablets using the declared content of $C_{13}H_{18}Cl_2N_2O_2$ in *melphalan BPCRS*.