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Bicalutamide Tablets

General Notices

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

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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Identification B** test deleted **Related substances** quantitative limits introduced & limits revised **Assay** column efficiency SST deleted

Action and use

Antiandrogen; treatment of prostate cancer.

DEFINITION

Bicalutamide Tablets contain Bicalutamide.

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

Content of bicalutamide, $C_{18}H_{14}F_4N_2O_4S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a quantity of the powdered tablets containing 0.1 g of Bicalutamide add 10 mL of *acetone*, shake and centrifuge. Filter the supernatant liquid (Whatman GF/C filter is suitable) and evaporate to dryness under a stream of nitrogen at 40° for 30 minutes. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of bicalutamide (*RS 466*).

TESTS

Dissolution

Comply with the requirements in 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 a 1.0% w/v solution of *sodium dodecyl sulfate*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with *water* if necessary, to produce a solution expected to contain 0.0056% w/v of Bicalutamide, at the maximum at 272 nm, Appendix II B using the dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.0056% w/v solution of *bicalutamide BPCRS* using the dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of bicalutamide, $C_{18}H_{14}F_4N_2O_4S$ in the medium from the absorbances obtained and using the declared content of $C_{18}H_{14}F_4N_2O_4S$ in *bicalutamide BPCRS*.

LIMITS

The amount of bicalutamide released is not less than 75% (Q) of the stated amount.

Related substances

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

Solution A 0.5 volumes *orthophosphoric acid*, 500 volumes of *acetonitrile R1* and 500 volumes of *water*.

(1) Disperse a quantity of the powdered tablets containing 25 mg of Bicalutamide in solution A with the aid of ultrasound. Add sufficient solution A to produce a solution containing 0.1% w/v of Bicalutamide and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes. Dilute 1 volume of this solution to 10 volumes.
(3) 0.1% w/v of *bicalutamide for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 50°.
(e) Use a detection wavelength of 210 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 1.9 volumes of *orthophosphoric acid*, 100 volumes of *acetonitrile R1* and 1900 volumes of *water*.

Mobile phase B 1.9 volumes of *orthophosphoric acid*, 100 volumes of *water* and 1900 volumes of *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-3	92	8	isocratic
3-23	92→67	8→33	linear gradient
23-43	67→50	33→50	linear gradient
43-55	50	50	isocratic
55-56	50→92	50→8	linear gradient
56-60	92	8	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak to valley ratio* is at least 2.5, where H_p is the height above the baseline of the peak due to impurity B and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to bicalutamide.

CALCULATION OF IMPURITIES

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

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

For peak identification, use solution (3).

Bicalutamide retention time: about 38 minutes.

Relative retentions: impurity D, about 0.7; impurity B, about 0.98 and impurity C, about 1.1.

LIMITS

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 0.7%;

— reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

Solution B 40 volumes of *water* and 60 volumes of *acetonitrile*.

(1) To a quantity of the powdered tablets containing 0.25 g of Bicalutamide, add 40 mL of *water* and mix with the aid of ultrasound, add sufficient *acetonitrile* to produce 100 mL and mix. Centrifuge and dilute 1 volume of the supernatant liquid to 25 volumes with solution B.
(2) 0.01% w/v of *bicalutamide BPCRS* in solution B.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (4 µm) (Novapak C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 270 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

1 volume of *trifluoroacetic acid*, 350 volumes of *acetonitrile* and 650 volumes of *water*.

When the chromatograms are recorded under the prescribed conditions, the retention time of bicalutamide is about 10 minutes.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{14}F_4N_2O_4S$ in the tablets using the declared content of $C_{18}H_{14}F_4N_2O_4S$ in *bicalutamide BPCRS*.

IMPURITIES

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