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

Pirfenidone Capsules

General Notices

(Ph. Eur. monograph 3154)

Action and use

Treatment of idiopathic pulmonary fibrosis.

Ph Eur

DEFINITION

Capsules containing *Pirfenidone (2856)*, for human use.

They comply with the monograph Capsules (0016) and the following additional requirements.

Content

95.0 per cent to 105.0 per cent of the content of pirfenidone ($C_{12}H_{11}NO$) stated on the label.

IDENTIFICATION

A. Record the UV spectrum of the principal peak in the chromatograms obtained with the solutions used in the assay with a diode array detector in the range of 210-400 nm.

Results The UV spectrum of the principal peak in the chromatogram obtained with the test solution is similar to the UV spectrum of the principal peak in the chromatogram obtained with reference solution (c).

B. Examine the chromatograms obtained in the assay.

Results The principal peak in the chromatogram obtained with the test solution is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (c).

TESTS

Related substances

Liquid chromatography (*2.2.29*).

Test solution Weigh 10 capsules and mix their contents. Weigh the capsule shells and determine the mean capsule fill mass. To an amount of powder close to the mean capsule fill mass, add 150 mL of mobile phase A and mix. Dilute to 250.0 mL with mobile phase A. Filter. Dilute with mobile phase A to obtain a concentration of pirfenidone of approximately 1.0 mg/mL.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with mobile phase A. Dilute 1.0 mL of this solution to 10.0 mL with mobile phase A.

Reference solution (b) Dissolve 5 mg of *5-methylpyridin-2-amine R* (impurity A) and 5 mg of *5-methylpyridin-2(1H)-one R* (impurity B) in *methanol R* and dilute to 100 mL with the same solvent. Dilute 1 mL of the solution to 100 mL with mobile phase A.

Reference solution (c) Dissolve 20.0 mg of *pirfenidone CRS* in mobile phase A and dilute to 200.0 mL with mobile phase A.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octylsilyl silica gel for chromatography R* (5 µm);

— *temperature*: 40 °C.

Mobile phase:

— *mobile phase A*: add 0.9 mL of *triethylamine R2* to 650 mL of *water for chromatography R* and adjust to pH 3.0 with *phosphoric acid R*. Mix 650 mL of this solution, 130 mL of *methanol R1* and 220 mL of *acetonitrile for chromatography R*;

— *mobile phase B*: *acetonitrile for chromatography R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 26	100	0
26 - 26.01	100 → 85	0 → 15
26.01 - 40	85	15
40 - 42	85 → 100	15 → 0

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 220 nm.

Injection 50 µL of the test solution and reference solutions (a) and (b).

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and B.

Relative retention With reference to pirfenidone (retention time = about 10 min): impurity A = about 0.2; impurity B = about 0.3.

System suitability Reference solution (b):

— *resolution*: minimum 3.0 between the peaks due to impurities A and B.

Calculation of percentage contents:

— for each impurity, use the concentration of pirfenidone in reference solution (a).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.3 per cent;

— *reporting threshold*: 0.05 per cent; disregard any peak due to the blank with a relative retention of about 0.28.

Dissolution

[1] (*2.9.3, Apparatus 2*). *Use sinker devices*.

Dissolution medium *water R*. Use 1000 mL of the medium.

Rotation speed 50 r/min.

Time 30 min.

Analysis Ultraviolet and visible absorption spectrophotometry (2.2.25) using a path length of 2 mm.

Test solutions Samples withdrawn from the dissolution vessel and filtered.

When a different path length is used, the solutions may be diluted accordingly (e.g. for a path length of 1 cm, 5-fold dilution for 267 mg capsules).

Measure the absorbances of the solutions at 312 nm.

Calculate the amount of dissolved pirfenidone ($C_{12}H_{11}NO$), expressed as a percentage of the content stated on the label, taking the specific absorbance to be 320.

Acceptance criterion:

— *Q* = 85 per cent after 30 min.

ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modifications.

Mobile phase Mobile phase A.

Injection 15 µL of the test solution and reference solution (c).

Run time 1.5 times the retention time of pirfenidone.

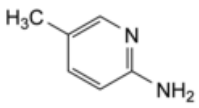
System suitability Reference solution (c):

— *repeatability*: maximum relative standard deviation of 1.0 per cent determined on 6 injections.

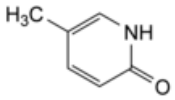
Calculate the percentage content of pirfenidone ($C_{12}H_{11}NO$) taking into account the assigned content of *pirfenidone CRS*.

IMPURITIES

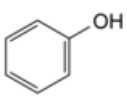
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph)*: A, B, C, D*.



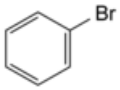
A. 5-methylpyridin-2-amine,



B. 5-methylpyridin-2(1*H*)-one,



C. phenol,



D. bromobenzene.

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1 The test approved in the marketing authorisation is to be used for routine quality control to confirm batch-to-batch consistency. For more information please consult Ph. Eur. 1. General Notices.