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Modafinil Tablets

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

EAG MC2	Medicinal Chemicals 2
Contact Details	helen.corns@mhra.gov.uk stephen.maddocks@mhra.gov.uk
Deadline for Comment	31 st September 2019
Target Publication Date (subject to change)	BP 2021
Notes:	New monograph

Action and use

Narcolepsy and sleep disorders

DEFINITION

Modafinil Tablets contain modafinil.

The tablets complies with the requirements stated under [Tablets](#) and with the following requirements.

Content of modafinil, $C_{33}H_{34}N_6O_6$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Boil a quantity of the powdered tablets containing 100 mg of Modafinil with 15 mL of acetone and filter the hot solution. Wash the filter paper with two 5-mL quantities of hot acetone and cool in ice. Evaporate the combined filtrates to dryness. The infrared absorption spectrum of the dried residue, [Appendix II A](#), is concordant with the reference spectrum of modafinil (RS XXX).

TESTS

Dissolution

Comply with the dissolution test for tablets and capsules, [Appendix XII B1](#).

TEST CONDITIONS

- Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
- 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 (a 0.45-µm filter is suitable). Dilute the filtered medium, if necessary, with sufficient dissolution medium to produce a solution expected to contain 0.01% w/v modafinil.
- (2) 0.01% of modafinil BPCRS in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column 150 cm × 4.6 mm packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Intersil ODS-2 is suitable).
- (b) Use isocratic elution and the mobile phase described below.
- (c) Use a flow rate of 1.0 mL per minute.
- (d) Use a column temperature of 40 °.
- (e) Use a detection wavelength of 220 nm.
- (f) Inject 20 µL of each solution.

MOBILE PHASE

350 volumes of [acetonitrile](#) and 650 volumes of a 0.68% w/v solution of [potassium dihydrogen orthophosphate](#), previously adjusted to pH 2.3 with [orthophosphoric acid](#).

When chromatograms are collected under the prescribed conditions, the retention time of modafinil is about 4 minutes.

DETERMINATION OF CONTENT

Calculate the total content of modafinil, C₃₃H₃₄N₆O₆, in the medium from the absorbances obtained and using the declared content of C₃₃H₃₄N₆O₆, in [modafinil BPCRS](#).

LIMITS

The amount of modafinil 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 in a mixture of 1 volume of a 5M solution of [acetic acid](#), 350 volumes of [acetonitrile](#) and 650 volumes of [water](#).

- (1) Mix, with the aid of ultrasound, a quantity of the powdered tablets containing 100 mg of Modafinil with 80 mL of the diluent and dilute to 100 mL. Filter the solution and dilute 1 volume to 10 volumes.
- (2) Dilute 1 volume of solution (1) to 200 volumes.
- (3) Add 2.0 mL of the diluent to a vial of [modafinil for system suitability EPCRS](#).
- (4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions stated under Dissolution may be used.

Record the chromatograms for 4 times the retention time of modafinil

MOBILE PHASE

350 volumes of [acetonitrile](#) and 650 volumes of a 0.68% w/v solution of [potassium dihydrogen orthophosphate](#), previously adjusted to pH 2.3 with [orthophosphoric acid](#).

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to modafinil (retention time about 4 minutes) are: impurity A, about 1.3; impurity B, about 1.8 and impurity C, about 3.0.

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 A and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to modafinil.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B or C is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5% of each);

the area of any other [secondary peak](#) is not greater than twice the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the sum of the areas of any [secondary peaks](#) is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions in a mixture of 1 volume of a 5M solution of [acetic acid](#), 350 volumes of [acetonitrile](#) and 650 volumes of [water](#).

(1) Mix, with the aid of ultrasound, a quantity of the powdered tablets containing 100 mg of Modafinil with 80 mL of the diluent and dilute to 100 mL. Dilute 1 volume of the resulting solution to 10 volumes.

(2) 0.01% w/v of [modafinil BPCRS](#).

(3) Add 2.0 mL of the diluent to a vial of [modafinil for system suitability EPCRS](#).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions stated under Dissolution may be used.

MOBILE PHASE

350 volumes of [acetonitrile](#) and 650 volumes of a 0.68% w/v solution of [potassium dihydrogen orthophosphate](#), previously adjusted to pH 2.3 with [orthophosphoric acid](#).

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 A and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to modafinil.

DETERMINATION OF CONTENT

Calculate the content of modafinil, $C_{34}H_{33}N_6O_6$, in the tablets from the chromatograms obtained and using the declared content of $C_{34}H_{33}N_6O_6$, in [modafinil BPCRS](#).

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under [Modafinil](#).

Draft monograph - Subject to change