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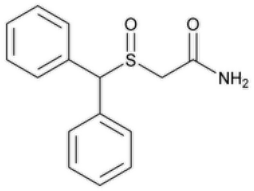
Modafinil



$C_{15}H_{15}NO_2S$ 273.35

Acetamide, 2-[(diphenylmethyl)sulfinyl]-;

2-[(Diphenylmethyl)sulfinyl]-acetamide CAS RN®: 68693-11-8; UNII: R3UK8X3U3D.

DEFINITION

Modafinil contains NLT 98.0% and NMT 101.5% of modafinil ($C_{15}H_{15}NO_2S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (USP 1-May-2021)

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

Buffer: 6.8 g/L of potassium dihydrogen phosphate in water. Adjust with phosphoric acid to a pH of 2.3.

Mobile phase: Acetonitrile and *Buffer* (35:65)

Diluent: Acetonitrile and water (35:65)

System suitability solution: 5 µg/mL of USP Modafinil RS and 10 µg/mL of USP Salicylic Acid RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Modafinil RS in *Diluent*

Sample solution: 0.1 mg/mL of Modafinil in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for modafinil and salicylic acid are about 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.3 between modafinil and salicylic acid

Tailing factor: NMT 1.5 for the modafinil peak

Relative standard deviation: NMT ▲0.73%▲ (USP 1-May-2021) for the modafinil peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of modafinil ($C_{15}H_{15}NO_2S$) in the portion of Modafinil taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of modafinil from the *Sample solution*

r_S = peak response of modafinil from the *Standard solution*

C_S = concentration of USP Modafinil RS in the *Standard solution* (mg/mL)

C_U = concentration of Modafinil in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–101.5% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, ▲Diluent,▲ (USP 1-May-2021) System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲Sensitivity solution: 0.05 µg/mL of USP Modafinil RS in *Diluent*▲ (USP 1-May-2021)

System suitability

Samples: *System suitability solution*▲and *Sensitivity solution*▲ (USP 1-May-2021)

Suitability requirements

Resolution: NLT 1.3 between modafinil and salicylic acid, ▲*System suitability solution*▲ (USP 1-May-2021)

Tailing factor: NMT 1.5 for the modafinil peak, ▲*System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-May-2021)

Analysis

Sample: *Sample solution*

Calculate the percentage of each ▲individual▲ (USP 1-May-2021) impurity in the portion of Modafinil taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response of each individual impurity

r_T = sum of the responses of all the peaks

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.05%.▲ (USP 1-May-2021)

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Modafinil	1.0	—	—
Salicylic acid[a]	1.1	—	—
Modafinil acid[b]	1.4	1.0	0.5
Modafinil sulfone[c]	1.7	0.9	0.5
Modafinil ester[d]	3.0	1.0	0.5
Any other individual unspecified impurity	—	1.0	0.05
Total impurities	—	—	1.0

[a] Salicylic acid is used for calculating resolution and is not a potential impurity.

[b] 2-[(Diphenylmethyl)sulfinyl]acetic acid.

[c] 2-[(Diphenylmethyl)sulfonyl]acetamide.

[d] 2-[(Diphenylmethyl)sulfinyl]acetic acid methyl ester.

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** NMT 0.2%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Modafinil RS

USP Salicylic Acid RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MODAFINIL	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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