Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-32E600BE-2DD9-44E7-9394-99D190D380B5_5_en-US
DOI: https://doi.org/10.31003/USPNF_M54523_05_01
DOI Ref: 099u8

Modafinil Tablets

DEFINITION
Modafinil Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of modafinil ($C_{15}H_{15}NO_2S$).

IDENTIFICATION

Change to read:

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

Standard: ▲▲ (USP 1-May-2021) Transfer a quantity, in milligrams, of USP Modafinil RS, equivalent to the labeled amount of modafinil, to a suitable container. Add 50 mL each of dichloromethane and water. Shake the mixture, and allow the layers to separate. Filter a portion of the lower (dichloromethane) layer, and evaporate to dryness, using a stream of nitrogen if necessary.▲▲ (USP 1-May-2021)

Sample: ▲▲ (USP 1-May-2021) Grind 1 Tablet, and add 50 mL each of dichloromethane and water. Shake the mixture, and allow the layers to separate. Filter a portion of the lower (dichloromethane) layer, and evaporate to dryness, using a stream of nitrogen if necessary. ▲▲ (USP 1-May-2021)

Acceptance criteria: Meet the requirements

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 A: Acetonitrile and water (35:65)

Diluent B: Acetonitrile, water, and acetic acid (35:65:1)

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

Standard solution: 0.4 mg/mL of USP Modafinil RS in *Diluent B*

Sample solution: ▲0.4 mg/mL of modafinil prepared as follows.▲ (USP 1-May-2021) Weigh and finely powder Tablets (NLT 20). Transfer a portion of the powder, equivalent to 100 mg of modafinil, to a 250-mL volumetric flask, add 200 mL of *Diluent B*, and sonicate for about 5 min with intermittent manual shaking. Dilute with *Diluent B* to volume, and mix. Pass ▲a portion▲ (USP 1-May-2021) through a suitable filter of 0.45-µm or finer pore size, and use the filtrate.

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: 1.0 mL/min

Injection volume: 5 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 2.0% for the modafinil peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of modafinil ($C_{15}H_{15}NO_2S$) in the portion of Tablets 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 = nominal concentration of modafinil in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: Prepare a solution having a known concentration of USP Modafinil RS in *Medium*.

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium* if necessary

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: Absorption maximum at about 222 nm

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage▲ (USP 1-May-2021) of modafinil ($C_{15}H_{15}NO_2S$) dissolved:

$$\text{▲Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)▲ (USP 1-May-2021)

Tolerances: NLT 75% (Q) of the labeled amount of modafinil ($C_{15}H_{15}NO_2S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: (L/900) mg/mL of USP Modafinil RS, where L is the label claim in mg/Tablet. Prepare by dissolving the standard in a volume of methanol equivalent to 5%–10% of the final volume and then diluting with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: Absorption maximum at about 225 nm

Cell: 0.1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of modafinil ($C_{15}H_{15}NO_2S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of modafinil ($C_{15}H_{15}NO_2S$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 900 mL, deaerated

Apparatus 2: 75 rpm

Time: 30 min

Standard solution: (L/900) mg/mL of USP Modafinil RS, where L is the label claim in mg/Tablet. Prepare by dissolving the standard in a volume of methanol equivalent to 5%–10% of the final volume and then diluting with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: Absorption maximum at about 220 nm

Cell: 0.1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of modafinil ($C_{15}H_{15}NO_2S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of modafinil ($C_{15}H_{15}NO_2S$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

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

▲Sensitivity solution: 0.4 µg/mL of USP Modafinil RS in *Diluent B*▲ (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)

Relative standard deviation: NMT 2.0% 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 impurity in the portion of Tablets 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 0.1%.▲ (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	0.90	0.5
Any individual unspecified impurity	—	1.0	0.2
Total impurities	—	—	1.5

[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.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.
- **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 TABLETS	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(5)

Current DocID: GUID-32E600BE-2DD9-44E7-9394-99D190D380B5_5_en-US

DOI: https://doi.org/10.31003/USPNF_M54523_05_01

DOI ref: 099u8