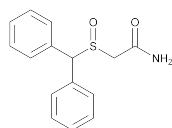


## Modafinil



$C_{15}H_{15}NO_2S$  273.35  
 Acetamide, 2-[(diphenylmethyl)sulfinyl]-;  
 2-[(Diphenylmethyl)sulfinyl]-acetamide [68693-11-8].

### DEFINITION

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

### IDENTIFICATION

- **A. INFRARED ABSORPTION** (197K)

### ASSAY

- **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 50 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 size:** 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 2.0% 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 from the Sample solution

$r_S$  = peak response 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:

- **HEAVY METALS**, Method II (IRA1-Sep-2011) (231): NMT 20 ppm

- (IRA 1-Sep-2011)

- **ORGANIC IMPURITIES**

**Buffer, Mobile phase, Sample solution, System suitability solution, and Chromatographic system:** Prepare as directed in the Assay.

#### System suitability

**Sample:** System suitability solution

#### 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

**Sample:** Sample solution

Calculate the percentage of each 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.

Table 1

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

<sup>a</sup> Salicylic acid is used for calculating resolution and is not a potential impurity.

<sup>b</sup> 2-[(Diphenylmethyl)sulfinyl]acetic acid.

<sup>c</sup> 2-[(Diphenylmethyl)sulfonyl]acetamide.

<sup>d</sup> 2-[(Diphenylmethyl)sulfinyl]acetic acid methyl ester.

### SPECIFIC TESTS

- **WATER DETERMINATION**, Method I (921): 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