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Repaglinide Tablets

DEFINITION
Repaglinide Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of repaglinide ($C_{27}H_{36}N_2O_4$).

IDENTIFICATION

• **A.** [Thin-Layer Chromatographic Identification Test ⟨201⟩]

Sample solution: To a quantity of powdered Tablets, equivalent to 10 mg of repaglinide, add 10 mL of a mixture of methanol and methylene chloride (1:1), shake for 15 min, and centrifuge.

Developing solvent system: Toluene, methylene chloride, and methanol (2:2:1)

Acceptance criteria: Meet the requirements

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **C.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer pH 4.0: 2 g/L of monobasic ammonium phosphate solution. Adjust with phosphoric acid to a pH of 4.0.

Buffer pH 2.5: 2 g/L of monobasic ammonium phosphate solution. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase: Methanol and *Buffer pH 2.5* (7:3)

Diluent: Methanol and *Buffer pH 4.0* (7:3)

Standard solution 1: 800 µg/mL of USP Repaglinide RS in methanol

Standard solution 2: 80 µg/mL of USP Repaglinide RS, prepared by diluting 5.0 mL of *Standard solution 1* with *Diluent* to 50.0 mL

System suitability stock solution: 80 µg/mL of USP Repaglinide Related Compound A RS in methanol

System suitability solution: 80 µg/mL of USP Repaglinide RS and 1.6 µg/mL of USP Repaglinide Related Compound A RS prepared as follows. Transfer 1.0 mL of *System suitability stock solution* to a 50-mL volumetric flask, add 5.0 mL of *Standard solution 1*, and dilute with *Diluent* to volume.

Sample solution: Transfer 8 whole Tablets to a suitable volumetric flask, and dissolve in and dilute with *Diluent* to volume to obtain a solution containing 80 µg/mL. Stir for 20 min, and filter or centrifuge a portion of the solution.

Chromatographic system

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

Mode: LC

Detector: UV 245 nm or diode array. [Note—Use diode array detector to perform *Identification* test *C*.]

Column: 4.0-mm × 6-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solution 2* and *System suitability solution*

[Note—The typical relative retention times for repaglinide related compound A and repaglinide are about 0.4 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 7.0 between repaglinide related compound A and repaglinide, *System suitability solution*

Tailing factor: 0.8–2.0 for the repaglinide peak, *System suitability solution*

Relative standard deviation: NMT 2.0% for replicate injections, *Standard solution 2*

Analysis

Samples: *Standard solution 2* and *Sample solution*

Calculate the percentage of the labeled amount of repaglinide ($C_{27}H_{36}N_2O_4$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from *Standard solution 2*

C_S = concentration of USP Repaglinide RS in *Standard solution 2* (µg/mL)

C_U = nominal concentration of repaglinide in the *Sample solution* (µg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: pH 5.0 buffer, prepared by mixing 10.2 g of citric acid monohydrate and 18.16 g of dibasic sodium phosphate dihydrate with 1 L of water; 900 mL

Apparatus 2: 75 rpm

Time: 30 min

Buffer: 1.5 g/L of monobasic potassium phosphate in water, adjusted with phosphoric acid to a pH of 2.3

Mobile phase: Acetonitrile, *Buffer,* and methanol (49:40:11)

Standard stock solution: 44 µg/mL of USP Repaglinide RS in methanol

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

Standard solution: Transfer 5.0 mL of the *Standard stock solution* to a 100-mL volumetric flask, add 25 mL of methanol, and dilute with *Medium* to volume. Further dilute with *Medium*, if needed, to a concentration that is similar to that of the *Sample solution*.

Chromatographic system

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

Mode: LC

Detector: Fluorometric detector; excitation wavelength of 244 nm and emission wavelength of 348 nm

Column: 4.0-mm × 12.5-cm; 10-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: Between 0.5 and 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of the labeled amount of repaglinide ($C_{27}H_{36}N_2O_4$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim of repaglinide (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 70% (Q) of the labeled amount of repaglinide ($C_{27}H_{36}N_2O_4$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Buffer pH 4.0, Buffer pH 2.5, Mobile phase, Diluent, Standard solution 1, Standard solution 2, System suitability stock solution, System suitability solution, and **Sample solution:** Prepare as directed in the *Assay*.

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Standard solution 3: 0.2 µg/mL of USP Repaglinide RS, prepared by diluting 2.5 mL of *Standard solution 2* with *Diluent* to 1000 mL

Chromatographic system

Mode: LC

Detector: UV 210 nm

Column: 4.0-mm × 6-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution 3*

[NOTE—The typical relative retention times for repaglinide related compound A and repaglinide are about 0.4 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 7.0 between repaglinide related compound A and repaglinide, *System suitability solution*

Tailing factor: 0.8–2.0 for the repaglinide peak, *System suitability solution*

Relative standard deviation: NMT 10% for replicate injections, *Standard solution 3*

Analysis

Samples: *Sample solution* and *Standard solution 3*

Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of repaglinide from *Standard solution 3*

C_S = concentration of USP Repaglinide RS in *Standard solution 3* (µg/mL)

C_U = nominal concentration of repaglinide in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.5% of total impurities

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **USP REFERENCE STANDARDS** ⟨11⟩

USP Repaglinide RS

USP Repaglinide Related Compound A RS

(*S*)-3-Methyl-1-[2-(1-piperidinyl)phenyl]butylamine, *N*-acetyl-L-glutamate salt.

$C_{16}H_{26}N_2 \cdot C_7H_{11}NO_5$ 435.6

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

Topic/Question	Contact	Expert Committee
REPAGLINIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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