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Risperidone Orally Disintegrating Tablets

DEFINITION

Risperidone Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of risperidone ($C_{23}H_{27}FN_4O_2$).

IDENTIFICATION

Change to read:

• **▲A.▲** (USP 1-MAY-2019) The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• B. The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

ASSAY

Change to read:

• **PROCEDURE**

Mobile phase: Acetonitrile, trifluoroacetic acid, and water (200:1.5:800). Adjust with ammonium hydroxide to a pH of 3.0.

Diluent: Methanol and 0.1 N hydrochloric acid (40:60)

System suitability solution: 0.1 mg/mL of USP Risperidone Related Compounds Mixture RS prepared as follows. ▲Transfer a suitable quantity of USP Risperidone Related Compounds Mixture RS to a suitable volumetric flask and dissolve▲ (USP 1-May-2019) in 20% of the flask volume of methanol. Dilute with *Diluent* to volume.

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

Sample solution: ▲Nominally▲ (USP 1-May-2019) 0.1 mg/mL of risperidone in *Diluent* from NLT 13 Tablets. [NOTE—Sonicate for 30 min.]

Chromatographic system

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

Mode: LC

Detector: UV 275 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2019)

Column: 3.0-mm × 15-cm; 3.5-µm packing L1

Flow rate: 0.8 mL/min

Injection volume: 10 µL

Run time: ▲NLT 2.2▲ (USP 1-May-2019) times the retention time of risperidone

System suitability

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

[NOTE—For relative retention times, see ▲*Table 1*.▲ (USP 1-May-2019)]

Suitability requirements

Resolution: NLT 1.8 between *Z*-oxime and bicyclorisperidone, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲the labeled amount of risperidone▲ (USP 1-May-2019) ($C_{23}H_{27}FN_4O_2$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Test 1: NMT 30 s

Test 2: NMT 60 s. [Note—If the product complies with this test, the labeling indicates that the product meets USP *Disintegration Test 2*.]

Change to read:

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 10 min

Buffer: 8.7 g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 7.8.

Mobile phase: Acetonitrile and *Buffer* (45:55)

Standard solution: (*L*/500) mg/mL of USP Risperidone RS in *Medium*, where *L* is the label claim in mg/Tablet

Sample solution: Pass 10 mL of the solution under test through a suitable ▲▲ (USP 1-May-2019) filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 10-cm; 5-µm packing L1

Column temperature: 28 ± 3°

Flow rate: 2 mL/min

Injection volume: 20 µL. [Note—Use 40 µL for Tablets labeled to contain 0.5 mg of risperidone.]

Run time: ▲NLT▲ (USP 1-May-2019) 2 times the retention time of risperidone

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲the labeled amount of risperidone▲ (USP 1-May-2019) ($C_{23}H_{27}FN_4O_2$) 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 the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of risperidone is dissolved.

Change to read:

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

▲▲ (USP 1-May-2019)

IMPURITIES

Change to read:

• **Organic Impurities**

Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Tablets taken:

$$\text{Result} = (r_{U1}/r_{U2}) \times (1/F) \times 100$$

r_{U1} = peak response of any individual impurity from the *Sample solution*

r_{U2} = peak response of risperidone from the *Sample solution*

F = relative response factor (see ▲▲ (USP 1-May-2019) *Table 1*)

Acceptance criteria: ▲See *Table 1*.▲ (USP 1-May-2019)

▲▲ (USP 1-May-2019) **Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Z-Oxime[a,b]	0.59	1.0	—
Bicyclorisperidone[c]	0.66	0.86	0.3
Risperidone	1.0	1.0	—
Risperidone *cis*-*N*-oxide[d]	1.7	0.97	0.5
Any unspecified degradation product	—	1.0	0.2
▲Total impurities	—	—	1.0▲ (USP 1-May-2019)

[a] Process impurity; it is used to establish system suitability only.

[b] (*Z*)-3-[2-[4-(2,4-Difluorophenyl)(hydroxyimino)methyl]-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4*H*-pyrido[1,2-a]pyrimidin-4-one.

[c] 3-(4-Fluoro-2-hydroxyphenyl)-1-[2-(6,7,8,9-tetrahydro-2-methyl-4-oxo-4*H*-pyrido-[1,2-a]pyrimidin-3-yl)ethyl]-2-aza-1-azoniabicyclo[2.2.2]oct-2-ene.

[d] *cis*-3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4*H*-pyrido[1,2-a]pyrimidin-4-one,*N*-oxide.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** When more than one *Disintegration* test is given, the labeling states the *Disintegration* test used only if *Test 1* is not used.

• **USP Reference Standards** ⟨11⟩

USP Risperidone RS

4*H*-Pyrido[1,2-*a*]pyrimidin-4-one, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-.
3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidino]ethyl]-6,7,8,9-tetrahydro-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one.
$C_{23}H_{27}FN_4O_2$ 410.48

USP Risperidone Related Compounds Mixture RS

Contains a mixture of the following four compounds:
Risperidone.
Risperidone *cis*-*N*-oxide: *cis*-3-[2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one, *N*-oxide.

Bicyclorisperidone: 3-(4-Fluoro-2-hydroxyphenyl)-1-[2-(6,7,8,9-tetrahydro-2-methyl-4-oxo-4*H*-pyrido-[1,2-*a*]pyrimidin-3-yl)ethyl]-2-aza-1-azoniabicyclo[2.2.2]oct-2-ene iodide.

Z-Oxime: (*Z*)-3-[2-[4-(2,4-Difluorophenyl)(hydroxyimino)methyl]-1-piperidinyl]ethyl-6,7,8,9-tetrahydro-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one.

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

Topic/Question	Contact	Expert Committee
RISPERIDONE ORALLY DISINTEGRATING TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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