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Paroxetine Extended-Release Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-paroxetine-ert-20220729.

DEFINITION

Paroxetine Extended-Release Tablets contain paroxetine hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$).

IDENTIFICATION

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

ASSAY

• **Procedure**

Buffer: 3.9 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 4.5.

Mobile phase: Acetonitrile, *Buffer*, and triethylamine (40:60:1). Adjust with glacial acetic acid to a pH of 5.5.

Standard solution: 0.5 mg/mL of USP Paroxetine Hydrochloride RS in methanol

System suitability solution: 0.5 mg/mL of USP Paroxetine Related Compound B RS in *Standard solution*

Sample solution: Nominally 0.5 mg/mL of paroxetine from NLT 10 Tablets prepared as follows. Transfer the required number of Tablets to a suitable volumetric flask. Add 80% of the flask volume of methanol. Sonicate for 30 min followed by stirring for 30 min. Dilute with methanol to volume.

Chromatographic system

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

Mode: LC

Detector: UV 295 nm

Column: 4.6-mm × 25-cm; 5-µm packing L13

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for paroxetine related compound B and paroxetine are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between paroxetine related compound B and paroxetine, *System suitability solution*

Tailing factor: NMT 2.0 for paroxetine, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Buffer stage medium: 0.05 M tris buffer prepared as follows. Dissolve 6.06 g of tris(hydroxymethyl)aminomethane in 1 L of water. Add 1.8 mL of hydrochloric acid to the resulting solution. Adjust with hydrochloric acid to a pH of 7.5; 1000 mL deaerated.

Apparatus 1: 100 rpm

Times: 2 h in *Acid stage*; 2, 4, and 12 h in *Buffer stage*

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

Acid stage standard stock solution: 0.33 mg/mL of paroxetine prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Dissolve in 5% of the flask volume of methanol. Dilute with *Acid stage medium* to volume.

Acid stage standard solution: Dilute the *Acid stage standard stock solution* with *Acid stage medium* to obtain a final concentration of (*L*/7500) mg/mL, where *L* is the label claim in mg.

Buffer stage standard stock solution: 0.25 mg/mL of paroxetine prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Dissolve in 5% of the flask volume of methanol. Dilute with *Buffer stage medium* to volume.

Buffer stage standard solution: Dilute the *Buffer stage standard stock solution* with *Buffer stage medium* to obtain a final concentration of (*L*/1000) mg/mL, where *L* is the label claim in mg.

Acid stage sample solution: Run the *Acid stage* for 2 h. Withdraw 10 mL of the solution under test and centrifuge. Use the centrifugate for analysis.

Buffer stage sample solution: Remove the *Acid stage medium* from the vessel and replace it with the *Buffer stage medium*. At the times specified, remove 10 mL of the solution under test and centrifuge. Use the centrifugate for analysis.

Chromatographic system: Proceed as directed in the *Assay*. For *Injection volume*, use 100 µL for the *Acid stage* analysis and 10 µL for the *Buffer stage* analysis.

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0, *Acid stage standard solution* and *Buffer stage standard solution*

Relative standard deviation: NMT 3.0%, *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved in the *Acid stage*:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

r_U = peak response from the *Acid stage sample solution*

r_S = peak response from the *Acid stage standard solution*

C_S = concentration of USP Paroxetine Hydrochloride RS in the *Acid stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

V = volume of the *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

Calculate the concentration (C_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point in the *Buffer stage*:

$$\text{Result} = (r_i/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_i = peak response from the *Buffer stage sample solution* at each time point *i*

r_S = peak response from the *Buffer stage standard solution*

C_S = concentration of USP Paroxetine Hydrochloride RS in the *Buffer stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Calculate the percentage of the labeled amount (Q_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (*i*) in the *Buffer stage medium*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of paroxetine in the *Buffer stage medium* in the portion of sample withdrawn at time point *i* (mg/mL)

V = volume of the *Buffer stage medium*, 1000 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Buffer stage medium* (mL)

Tolerances

Acid stage: NMT 10% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) is dissolved in 2 h.

Buffer stage: See *Table 1*.

Table 1

Time Point (*i*)	Time (h)	Amount Dissolved (Tablets labeled to contain 12.5 mg of paroxetine)	Amount Dissolved (Tablets labeled to contain 25 mg of paroxetine)	Amount Dissolved (Tablets labeled to contain 37.5 mg of paroxetine)
1	2	15%–35%	10%–30%	20%–45%
2	4	40%–70%	40%–70%	60%–85%
3	12	NLT 80%	NLT 80%	NLT 80%

The percentages of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

Test 2

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

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Buffer stage medium: 0.05 M tris buffer prepared as follows. Dissolve 6.06 g of tris(hydroxymethyl)aminomethane in 900 mL of water. Add 40 mL of 1.0 M hydrochloric acid to the resulting solution. Adjust with either 1.0 M hydrochloric acid or 1.0 M sodium hydroxide to a pH of 7.5. Dilute with water to 1 L; 1000 mL deaerated.

Apparatus 2: 150 rpm with suitable sinkers

Times: 2 h in *Acid stage*; 1, 2, 4, and 6 h in *Buffer stage*

Acid stage standard stock solution: 0.04 mg/mL of USP Paroxetine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Dissolve in 2 mL of methanol. Dilute with *Acid stage medium* to volume.

Acid stage standard solution: Dilute the *Acid stage standard stock solution* with *Acid stage medium* to obtain a final concentration of (*L*/7500) mg/mL of paroxetine, where *L* is the label claim in mg.

Buffer stage standard solution: (*L*/1000) mg/mL of paroxetine, where *L* is the label claim in mg prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Dissolve in 2 mL of methanol. Dilute with *Buffer stage medium* to volume.

Acid stage sample solution: Run the *Acid stage* for 2 h. Withdraw 10 mL of the solution under test, and filter. Use the filtrate for analysis.

Buffer stage sample solution: Remove the Tablet and sinker from the acid stage vessel and pat them dry. Introduce the Tablet and sinker into the dissolution vessel with 1000 mL of the *Buffer stage medium*. At the times specified, remove 10 mL of the solution under test and filter. Use the filtrate for analysis.

Acid stage analysis

Buffer: Add 2.9 mL of phosphoric acid to 800 mL of water. Adjust with 1 M sodium hydroxide to a pH of 6.0. Dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Chromatographic system

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

Mode: LC

Detector: UV 205 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 50 µL for 12.5-mg Tablet; 20 µL for 25- and 37.5-mg Tablets

Run time: 2 times the retention time of paroxetine

System suitability

Sample: *Acid stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved in the *Acid stage*:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times V \times (1/L) \times 100$$

r_U = peak response from the *Acid stage sample solution*

r_S = peak response from the *Acid stage standard solution*

C_S = concentration of USP Paroxetine Hydrochloride RS in the *Acid stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

V = volume of the *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

Buffer stage analysis

Instrumental conditions

Mode: UV

Analytical wavelength: 294 nm with 340 nm for background correction

Blank: *Buffer stage medium*

Analysis

Samples: *Buffer stage standard solution* and *Buffer stage sample solution*

Calculate the concentration (C_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (i) in the *Buffer stage*:

$$\text{Result} = (A_i/A_S) \times C_S \times (M_{r1}/M_{r2})$$

A_i = absorbance of the *Buffer stage sample solution* at time point *i*

A_S = absorbance of the *Buffer stage standard solution*

C_S = concentration of USP Paroxetine Hydrochloride RS in the *Buffer stage standard solution* (mg/mL)

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (*i*) in the *Buffer stage medium*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of paroxetine in the *Buffer stage medium* in the portion of sample withdrawn at time point *i* (mg/mL)

V = volume of the *Buffer stage medium*, 1000 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn from the *Buffer stage medium* (mL)

Tolerances

Acid stage: NMT 10% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) is dissolved in 2 h.

Buffer stage: See *Table 2*.

Table 2

Time Point (*i*)	Time (h)	Amount Dissolved
1	1	NMT 20%
2	2	20%–45%
3	4	60%–90%
4	6	NLT 85%

The percentages of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

Test 3

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

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Buffer stage medium: 0.05 M tris buffer prepared as follows. Dissolve 42 g of tris(hydroxymethyl)aminomethane in 2000 mL of water. Pass through a suitable filter of 0.45-µm pore size. Add 5000 mL of water and adjust with hydrochloric acid to a pH of 7.5; 1000 mL deaerated.

Apparatus 2: 150 rpm with suitable sinkers

Times: 2 h in *Acid stage*; 2, 4, and 6 h in *Buffer stage*

Solution A: 1.36 g/L of potassium phosphate monobasic and 2.44 g/L of sodium 1-decanesulfonate in water. Adjust with 0.5% phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Solution A* (45:55)

Standard stock solution: 0.042 mg/mL of USP Paroxetine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Add about 50% of the final flask volume of *Buffer stage medium* and sonicate for about 15 min to dissolve. Dilute with *Buffer stage medium* to volume.

Standard solution: 0.021 mg/mL of USP Paroxetine Hydrochloride RS prepared as follows. Mix equal portions of *Standard stock solution* and *Acid stage medium* in a suitable glass container.

Acid stage sample solution: Run the *Acid stage* for 2 h. Withdraw 10 mL of the solution under test. Centrifuge to obtain a clear supernatant. Mix equal portions of the supernatant and *Acid stage medium* in a suitable glass container. Use the resulting solution for analysis.

Buffer stage sample solution: Remove the Tablet in the sinker from the acid stage vessel. Add the Tablet in the sinker to the vessel with 1000 mL of *Buffer stage medium* and run the *Buffer stage*. At the times specified, remove 10 mL of the solution under test. Centrifuge to obtain a clear supernatant. Mix equal portions of the supernatant and *Acid stage medium* in a suitable glass container. Use the resulting solution for analysis.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: About 1.5 times the retention time of paroxetine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved in the *Acid stage*:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times D \times V \times (1/L) \times 100$$

r_U = peak response from the *Acid stage sample solution*

r_S = peak response from the *Standard solution*

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

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

D = dilution factor

V = volume of the *Acid stage medium*, 750 mL

L = label claim (mg/Tablet)

Calculate the concentration (C_i) of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (i) in the *Buffer stage*:

$$\text{Result}_i = (r_i/r_S) \times C_S \times (M_{r1}/M_{r2}) \times D$$

r_i = peak response from the *Buffer stage sample solution* at time point i

r_S = peak response from the *Standard solution*

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

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

D = dilution factor

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (i) in the *Buffer stage medium*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of paroxetine in the *Buffer stage medium* in the portion of sample withdrawn at time point *i* (mg/mL)

V = volume of the *Buffer stage medium*, 1000 mL

L = label claim (mg/Tablet)

V_S = volume of the sample solution withdrawn from the *Buffer stage medium* (mL)

Tolerances

Acid stage: NMT 10% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) is dissolved.

Buffer stage: See *Table 3*.

Table 3

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	20–50
2	4	55–85
3	6	NLT 80

The percentages of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at the times specified conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

▲**Test 4**

If the product complies with this procedure, the labeling indicates that it meets USP *Dissolution Test 4*.

Acid stage medium: 0.1 N hydrochloric acid; 750 mL

Buffer stage medium: 6.05 g/L of tris(hydroxymethyl)aminomethane in water. Adjust with hydrochloric acid to a pH of 7.5; 1000 mL.

Apparatus 2: 150 rpm

Times: 2 h in *Acid stage*; 2, 4, and 8 h in *Buffer stage*

Solution A: 3.85 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 4.5.

Mobile phase: Acetonitrile, *Solution A*, and triethylamine (35:65:1). Adjust with glacial acetic acid to a pH of 5.5.

Acid stage standard stock solution: 0.190 mg/mL of USP Paroxetine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Add 4% of the flask volume of methanol and sonicate to dissolve. Dilute with *Acid stage medium* to volume.

Acid stage standard solution: 0.019 mg/mL of USP Paroxetine Hydrochloride RS from *Acid stage standard stock solution* in *Acid stage medium*

Buffer stage standard stock solution: 0.142 mg/mL of USP Paroxetine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Paroxetine Hydrochloride RS to a suitable volumetric flask. Add 4% of the flask volume of methanol and sonicate to dissolve. Dilute with *Buffer stage medium* to volume.

Buffer stage standard solution: 0.0142 mg/mL of USP Paroxetine Hydrochloride RS from *Buffer stage standard stock solution* in *Buffer stage medium*

Acid stage sample solution: At the time specified, withdraw 10 mL of the solution under test and pass through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of filtrate. Dilute, if needed, with *Acid stage medium* to a concentration that is similar to that of the *Acid stage standard solution*.

Buffer stage sample solution: Remove the *Acid stage medium* from the vessel and replace it with the *Buffer stage medium*. At the times specified, withdraw 10 mL of the solution under test and replace with 10 mL of *Buffer stage medium*. Pass the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of filtrate. Dilute, if needed, with *Buffer stage medium* to a concentration that is similar to that of the *Buffer stage standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 295 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Temperatures

Autosampler: 10°

Column: 35°

Flow rate: 1.2 mL/min

Injection volume: 100 µL

Run time: NLT 2 times the retention time of paroxetine

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2, *Acid stage standard solution* and *Buffer stage standard solution*

Relative standard deviation: NMT 2.0%, *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved in the *Acid stage* (Q_A):

$$\text{Result} = (r_U/r_S) \times C_S \times V \times D \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of paroxetine from the *Acid stage sample solution*

r_S = peak response of paroxetine from the *Acid stage standard solution*

C_S = concentration of USP Paroxetine Hydrochloride RS in the *Acid stage standard solution* (mg/mL)

V = volume of the *Acid stage medium*, 750 mL

D = dilution factor for the *Acid stage sample solution*

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

L = label claim (mg/Tablet)

Calculate the concentration (C_i) of paroxetine ($C_{19}H_{20}FNO_3$) in the sample withdrawn from the vessel at each time point (i) in the *Buffer stage*:

$$\text{Result}_i = (r_i/r_S) \times C_S \times D \times (M_{r1}/M_{r2})$$

r_i = peak response of paroxetine from the *Buffer stage sample solution*

r_S = peak response of paroxetine from the *Buffer stage standard solution*

C_S = concentration of USP Paroxetine Hydrochloride RS in the *Buffer stage standard solution* (mg/mL)

D = dilution factor for the *Buffer stage sample solution*

M_{r1} = molecular weight of paroxetine, 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Calculate the percentage of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at each time point (i) in the *Buffer stage*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100 + Q_A$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100 + Q_A$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100 + Q_A$$

C_i = concentration of paroxetine in the portion of sample withdrawn at time point i (mg/mL)

V = volume of the *Buffer stage medium*, 1000 mL

L = label claim (mg/Tablet)

Q_A = percentage of the labeled amount of paroxetine dissolved in the *Acid stage*

V_S = volume of the sample solution withdrawn at each time point and replaced with *Buffer stage medium* (mL)

Tolerances

Acid stage: NMT 25% of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) is dissolved.

Buffer stage: See *Table 4*.

Table 4

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	23–43
2	4	50–70
3	8	NLT 80

The percentages of the labeled amount of paroxetine ($C_{19}H_{20}FNO_3$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.▲ (RB 1-Aug-2022)

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

IMPURITIES

Change to read:

• **Organic Impurities**

Solution A: Tetrahydrofuran, water, and trifluoroacetic acid (20:180:1)

Solution B: Acetonitrile, tetrahydrofuran, and trifluoroacetic acid (180:20:1)

Mobile phase: See ▲*Table 5*.

Table 5▲ (RB 1-Aug-2022)

Time (min)	Solution A (%)	Solution B (%)
0	80	20
30	80	20
50	20	80
60	20	80
70	80	20
80	80	20

System suitability solution: 1 mg/mL of USP Paroxetine Hydrochloride RS, 0.1 mg/mL of USP Paroxetine System Suitability Mixture A RS, and 1 mg/mL of USP Paroxetine Related Compound F RS in methanol. [Note—Sonication may be used to aid dissolution of the individual components.]

Standard solution: 0.01 mg/mL of USP Paroxetine Hydrochloride RS in methanol

Sample solution: Nominally 1 mg/mL of paroxetine from NLT 10 Tablets prepared as follows. Transfer a suitable number of Tablets to a suitable volumetric flask. Add 50% of the flask volume of methanol. Sonicate for 30 min followed by stirring for 30 min. Dilute with methanol to volume. Mix and centrifuge. Use the clear centrifugate.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE—See ▲*Table 6*▲ (RB 1-Aug-2022) for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between paroxetine related compound A and paroxetine related compound B; NLT 1.5 between paroxetine related compound F and paroxetine, *System suitability solution*

Tailing factor: NMT 2.0 for paroxetine, *Standard solution*

Relative standard deviation: NMT 5.0% for paroxetine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of paroxetine 329.37

M_{r2} = molecular weight of paroxetine hydrochloride, 365.83

Acceptance criteria: See ▲*Table 6*.

Table 6▲ (RB 1-Aug-2022)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Paroxetine related compound A[a]	0.67	—
Paroxetine related compound B[a]	0.75	—
Paroxetine related compound F[a]	0.90	—
Paroxetine	1.0	—
Ethoxyparoxetine[b]	1.2	0.2
Any unspecified degradation product	—	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Total impurities	—	1.0

[a] Process impurities, included for identification only. Process impurities are controlled in the drug substance and are not to be reported or included in the total impurities of the drug product.

[b] (3*SR*,4*RS*)-3-(1,3-Benzodioxol-5-yloxy)methyl)-4-(4-ethoxyphenyl)piperidine.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Paroxetine Hydrochloride RS

USP Paroxetine Related Compound B RS

trans-4-Phenyl-3-[(3,4-methylenedioxy)phenoxy]methylpiperidine hydrochloride;
Also known as Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-phenyl-, hydrochloride (3*S*-*trans*).
$C_{19}H_{21}NO_3 \cdot HCl$ 347.84

USP Paroxetine Related Compound F RS

(3S,4R)-3-[(Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-methylpiperidine.
$C_{20}H_{22}FNO_3$ 343.39

USP Paroxetine System Suitability Mixture A RS

Mixture of approximately 1% paroxetine related compound A [piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-methoxyphenyl)-, hydrochloride (3*S*-*trans*)], and 1% paroxetine related compound B [piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-phenyl-, hydrochloride (3*S*-*trans*)] in a matrix of paroxetine hydrochloride.

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

Topic/Question	Contact	Expert Committee
PAROXETINE EXTENDED-RELEASE 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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