

## Citalopram Tablets

### DEFINITION

Citalopram Tablets contain an amount of citalopram hydrobromide equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of citalopram free base ( $C_{20}H_{21}FN_2O$ ).

### IDENTIFICATION

#### A. INFRARED ABSORPTION (197K)

**Sample:** Extract finely ground Tablet powder containing 200 mg of citalopram with 30 mL of water, and filter. Add 1 mL of 1 N sodium hydroxide to the filtrate, and extract with 50 mL of cyclohexane by shaking for 10 min. Pass the cyclohexane layer through a silicone-treated filter paper into a beaker. Reduce the filtrate down to 3 mL, using gentle heat as necessary. Transfer the hot solution to a small centrifuge tube. Induce crystallization while cooling by scratching the side of the test tube with a spatula. Centrifuge the mixture, and decant off the cyclohexane. Dry the residue under vacuum in a desiccator. [NOTE—If crystallization fails to occur in the above procedure, use the following alternative procedure. Extract finely ground Tablet powder containing about 50 mg of citalopram with 10 mL of chloroform in a test tube, and sonicate for 1 min. Centrifuge for 10 min, and filter into a beaker. Evaporate to dryness with nitrogen and, if necessary, induce crystallization by etching the beaker.] Mix approximately 2 mg of the residue with approximately 300 mg of potassium bromide, and record the IR spectrum.

**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*.

### ASSAY

#### Change to read:

#### PROCEDURE

**Buffer:** 1.42 g/L of anhydrous dibasic sodium phosphate in water

**Diluent:** Methanol and *Buffer* (80:20)

**Mobile phase:** 0.77 mg/mL of dodecyltrimethylammonium bromide in *Diluent*

**Internal standard solution:** 0.25 mg/mL of USP Citalopram Related Compound F RS in *Diluent*

**Standard stock solution:** 1.25 mg/mL of USP Citalopram Hydrobromide RS in *Diluent*

**Standard solution:** 0.025 mg/mL of USP Citalopram Related Compound F RS and 0.125 mg/mL of USP Citalopram Hydrobromide RS from the *Internal standard solution* and the *Standard stock solution*, respectively, in *Diluent*

**Sample solution:** Transfer 10 Tablets to a 200-mL volumetric flask, add 25 mL of *Buffer*, and shake by mechanical means until disintegrated. Add 100 mL of methanol, and sonicate for about 5 min. Allow to cool to room temperature, and then dilute with *Diluent* to volume. Before taking an aliquot for dilution, allow to stand until the residue settles. Transfer a volume of the clear supernatant to a 50-mL volumetric flask to obtain a final nominal concentration between 0.090 and 0.10 mg/mL of citalopram. Add 5.0 mL of *Internal standard solution*, and dilute with *Diluent* to volume. Pass a portion through a filter (PTFE) having a 0.45- $\mu$ m or finer pore size.

### Chromatographic system

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

**Mode:** LC

**Detector:** UV 254 nm

**Column:** 4.6-mm  $\times$  25-cm; 5- $\mu$ m packing L1

**Column temperature:** 45°

**Flow rate:** 1 mL/min

**Injection volume:** 10  $\mu$ L

### System suitability

**Sample:** *Standard solution*

[NOTE—The relative retention times for citalopram related compound F and citalopram are about 1.36 and 1.0, respectively.]

### Suitability requirements

**Resolution:** NLT 1.5 between citalopram and citalopram related compound F

**Column efficiency:** NLT 2000 theoretical plates, calculated from the citalopram peak

**Relative standard deviation:** NMT 1.5% for the peak response ratio of citalopram to the internal standard. (IRA 1-May-2013)

### Analysis

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

Calculate the percentage of the labeled amount of citalopram ( $C_{20}H_{21}FN_2O$ ) 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 ratio of citalopram to the internal standard from the *Sample solution*

$R_S$  = peak response ratio of citalopram to the internal standard from the *Standard solution*

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

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

$M_{r1}$  = molecular weight of citalopram, 324.39

$M_{r2}$  = molecular weight of citalopram hydrobromide, 405.30

**Acceptance criteria:** 90.0%–110.0%

### PERFORMANCE TESTS

#### DISSOLUTION (711)

**Buffer:** pH 1.5 buffer (prepared by transferring 118 mL of 1 N hydrochloric acid and 82 mL of 1 N sodium hydroxide to a 1000-mL volumetric flask, diluting with water to volume, and adjusting with 1 N sodium hydroxide to a pH of 1.5)

**Medium:** *Buffer*; 800 mL, deaerated

**Apparatus 1:** 100 rpm

**Time:** 30 min

**Standard solution:** 12  $\mu$ g/mL of USP Citalopram Hydrobromide RS in *Medium*

**Sample solution:** Sample per *Dissolution* (711). Pass through a PVDF filter having a 0.45- $\mu$ m pore size, and dilute with *Medium* as needed.

### Instrumental conditions

(See *Spectrophotometry and Light-Scattering* (851).)

**Mode:** UV

**Analytical wavelength:** 239 nm

### Analysis

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

Calculate the percentage of the labeled amount of citalopram ( $C_{20}H_{21}FN_2O$ ) dissolved:

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

$A_U$  = absorbance of the *Sample solution*

$A_S$  = absorbance of the *Standard solution*

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

## 2 Citalopram

$V$  = volume of *Medium*, 800 mL  
 $D$  = dilution factor of the *Sample solution*  
 $M_{r1}$  = molecular weight of citalopram, 324.39  
 $M_{r2}$  = molecular weight of citalopram hydrobromide, 405.30  
 $L$  = label claim of citalopram (mg/Tablet)

**Tolerances:** NLT 80% (Q) of the labeled amount of citalopram (C<sub>20</sub>H<sub>21</sub>FN<sub>2</sub>O) is dissolved.

- **UNIFORMITY OF DOSAGE UNITS <905>**: Meet the requirements

### IMPURITIES

#### Change to read:

#### • ORGANIC IMPURITIES

**Buffer:** 3.15 g/L of monobasic potassium phosphate and 3.60 g/L of dibasic sodium phosphate dodecahydrate (Na<sub>2</sub>HPO<sub>4</sub> · 12H<sub>2</sub>O) in water

**Mobile phase:** Methanol, acetonitrile, and *Buffer* (38:7:55). Adjust with phosphoric acid to a pH of 6.5.

**Standard stock solution:** 0.25 mg/mL of USP Citalopram Hydrobromide RS in *Mobile phase*

**System suitability solution:** 1 µg/mL each of USP Citalopram Related Compound A RS, USP Citalopram Related Compound B RS, USP Citalopram Related Compound C RS, and USP Citalopram Related Compound E RS in the *Standard stock solution*

**Standard solution:** 0.625 µg/mL of citalopram hydrobromide from the *Standard stock solution* in *Mobile phase*

**Sensitivity solution:** 0.05 µg/mL of citalopram hydrobromide from the *Standard solution* in *Mobile phase*

**Sample solution:** Transfer 10 Tablets to a 200-mL volumetric flask, add 25 mL of *Buffer*, and shake by mechanical means until disintegrated. Add 100 mL of a mixture of methanol and water (1:1), mix, and sonicate for about 5 min. Allow to cool, dilute with a mixture of methanol and water (1:1) to volume, and mix thoroughly. Allow the excipients to settle. Dilute with *Mobile phase*, as necessary, to a final concentration of 0.5 mg/mL of citalopram. Pass a portion of this solution through a polytetrafluoroethylene (PTFE) membrane filter having a 0.45-µm or finer pore size, and use the filtrate.

#### Chromatographic system

(See *Chromatography <621>*, *System Suitability*.)

**Mode:** LC

**Detector:** UV 239 nm

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

**Column temperature:** 45°

**Flow rate:** 0.8 mL/min

**Injection volume:** 20 µL

#### System suitability

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

[NOTE—See *Table 1* for the relative retention times.]

#### Suitability requirements

**Resolution:** NLT 3 between citalopram related compound C and citalopram, *System suitability solution*

**Tailing factor:** NMT 1.5, *Standard solution*

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

**Signal-to-noise ratio:** NLT 3, *Sensitivity solution*

#### Analysis

**Samples:** • *System suitability solution*, • (IRA 1-May-2013) *Standard solution*, and *Sample solution*

• Chromatograph the *System suitability solution*, and identify the components on the basis of their relative retention times given in *Table 1*. • (IRA 1-May-2013)

Calculate the percentage of each impurity in the portion of Tablets • (IRA 1-May-2013) taken:

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

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

$r_S$  = peak response of the corresponding peak from the *Standard solution*

$C_S$  = concentration of citalopram hydrobromide in the *Standard solution* (mg/mL)

$C_U$  = nominal concentration of citalopram • (IRA 1-May-2013) in the *Sample solution* (mg/mL)

$M_{r1}$  = molecular weight of citalopram, 324.39

$M_{r2}$  = molecular weight of citalopram hydrobromide, 405.30

$F$  = relative response factor (see *Table 1*)

**Acceptance criteria:** See *Table 1*.

**Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Citalopram related compound A	0.43	0.77	0.2
Citalopram related compound B	0.60	0.98	0.25
Citalopram related compound C	0.83	0.69	0.25
Citalopram	1.0	—	—
Citalopram related compound E	1.32	0.91	0.1
Any other individual, unidentified impurity	—	1.0	0.2
Total impurities	—	—	0.8

### ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.

#### Change to read:

#### • USP REFERENCE STANDARDS <11>

USP Citalopram Hydrobromide RS

USP Citalopram Related Compound A RS

• 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carboxamide. • (IRA 1-May-2013)  
 C<sub>20</sub>H<sub>23</sub>FN<sub>2</sub>O<sub>2</sub> 342.22

USP Citalopram Related Compound B RS

• 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-3-hydroxy-1,3-dihydroisobenzofuran-5-carbonitrile oxalate.

C<sub>20</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>2</sub> · C<sub>2</sub>H<sub>2</sub>O<sub>4</sub> 430.43 • (IRA 1-May-2013)

USP Citalopram Related Compound C RS

• 3-(3-Dimethylaminopropyl)-3-(4-fluorophenyl)-6-cyano-1(3H)-isobenzofuranone oxalate.

C<sub>20</sub>H<sub>19</sub>FN<sub>2</sub>O<sub>2</sub> · C<sub>2</sub>H<sub>2</sub>O<sub>4</sub> 428.42 • (IRA 1-May-2013)

USP Citalopram Related Compound E RS

• 1-(3-Dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydrobenzofuran-5-carbonitrile-N-oxide hydrochloride.

C<sub>20</sub>H<sub>21</sub>FN<sub>2</sub>O<sub>2</sub> · HCl 376.85 • (IRA 1-May-2013)

USP Citalopram Related Compound F RS  
 Dimethyl-(1-methyl-3,3-diphenylallyl)amine hydrochloride.

C<sub>18</sub>H<sub>21</sub>N · HCl • 287.83 • (IRA 1-May-2013)