

Imipramine Pamoate Capsules

DEFINITION
Imipramine Pamoate Capsules contain imipramine pamoate [(C₁₉H₂₄N₂)₂ · C₂₃H₁₆O₆] equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of imipramine hydrochloride (C₁₉H₂₄N₂ · HCl).

IDENTIFICATION

- **A.** The retention time of the imipramine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the imipramine peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the test for *Organic Impurities*.

ASSAY

Change to read:

• **PROCEDURE**

Buffer: 5.2 g/L of [dibasic potassium phosphate](#) in water

Solution A: ▲[Acetonitrile](#)▲ (ERR 1-May-2019) and *Buffer* (15:85). Adjust with [phosphoric acid](#) to a pH of 8.0.

Solution B: ▲[Acetonitrile](#)▲ (ERR 1-May-2019) and *Buffer* (38:62). Adjust with [phosphoric acid](#) to a pH of 8.0.

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
10	70	30
20	35	65
30	35	65
31	90	10
35	90	10

Diluent: ▲[Acetonitrile](#)▲ (ERR 1-May-2019) and water (75:25)

Standard stock solution: 0.75 mg/mL of [USP Imipramine Pamoate RS](#) in *Diluent*

Standard solution: 0.23 mg/mL of [USP Imipramine Pamoate RS](#) (equivalent to 0.15 mg/mL of imipramine hydrochloride) from the *Standard stock solution* in *Solution A*. Pass a portion through a suitable filter of 0.45-µm pore size. Use the filtrate.

Sample stock solution: Transfer the contents of Capsules (NLT 5) into a suitable volumetric flask, and add the corresponding Capsule shells. Add 10% of the final flask volume of acetonitrile, and sonicate for 10 min with intermittent shaking. Add 80% of the final flask volume of *Diluent*, and sonicate for 15 min with intermittent shaking. Allow to cool to room temperature, and dilute with *Diluent* to volume. Allow to stand for 5 min.

Sample solution: Nominally 0.23 mg/mL of imipramine pamoate (equivalent to 0.15 mg/mL of imipramine hydrochloride) from the *Sample stock solution* in *Solution A*. Pass a portion of the resulting solution through a suitable filter of 0.45-µm pore size. Use the filtrate.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 269 nm

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

Autosampler temperature: 10°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for pamoic acid and imipramine are 0.3 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between pamoic acid and imipramine

Tailing factor: NMT 2.0 for imipramine

Relative standard deviation: NMT 2.0% for imipramine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) in the portion of Imipramine Pamoate Capsules taken:

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

r_U = peak area of imipramine from the *Sample solution*

r_S = peak area of imipramine from the *Standard solution*

C_S = concentration of [USP Imipramine Pamoate RS](#) in the *Standard solution* (mg/mL)

C_U = equivalent concentration of imipramine hydrochloride in the *Sample solution* (mg/mL)

M = number of moles of imipramine hydrochloride equivalent to each mole of imipramine pamoate, 2

M_{r1} = molecular weight of imipramine hydrochloride, 316.87

M_{r2} = molecular weight of imipramine pamoate, 949.18

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Tier 1

Medium 1: [0.1 N hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Times: 30 and 90 min

Tier 2

Medium 2: [0.1 N hydrochloric acid](#) with 0.3% [purified pepsin](#); 900 mL

Apparatus 1: 100 rpm

Times: 30 and 90 min

Buffer: 4.4 g/L of [dibasic potassium phosphate](#) in water

Mobile phase: [Acetonitrile](#), [triethylamine](#), and *Buffer* (400:5:600). Adjust with [phosphoric acid](#) to a pH of 8.0.

Diluent A: [Acetonitrile](#) and water (75:25)

Diluent B: 20.4 g/L of [monobasic potassium phosphate](#) and 3 g/L of [sodium hydroxide](#). Adjust with [1 N sodium hydroxide](#) or [1 N phosphoric acid](#) to a pH of 7.4.

Standard stock solution: 0.63 mg/mL of [USP Imipramine Pamoate RS](#) in *Diluent A*

Standard solution: 0.038 mg/mL of [USP Imipramine Pamoate RS](#) from the *Standard stock solution* prepared as follows. Transfer a suitable volume of the *Standard stock solution* to an appropriate flask that already contains 60% of the final flask volume of *Diluent B* and 30% of the final flask volume of *Medium*. Dilute with *Diluent B* to volume.

Sample stock solution: Centrifuge a portion of the solution under test. Use the supernatant. Replace the portion of solution removed from the vessel with the same volume of fresh *Medium 1* or *Medium 2* at 37°. [NOTE—The use of a centrifuge speed of 5000 rpm for 10 min may

be suitable.]

Sample solution: Nominally equivalent to about 0.025 mg/mL of imipramine hydrochloride prepared from the *Sample stock solution* in *Diluent B* in a suitable volumetric flask

Dissolution procedure: Perform the test using the conditions under *Tier 1*. In the presence of cross-linking, repeat the test with a new set of Capsules using the conditions under *Tier 2*.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 252 nm

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

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1.2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_i = (r_i/r_s) \times C_s \times [M \times (M_{r1}/M_{r2})] \times D \times V \times (1/L) \times 100$$

- r_i = peak area of imipramine from the *Sample solution* at each time point
- r_s = peak area of imipramine from the *Standard solution*
- C_s = concentration of [USP Imipramine Pamoate RS](#) in the *Standard solution* (mg/mL)
- M = number of moles of imipramine hydrochloride equivalent to each mole of imipramine pamoate, 2
- M_{r1} = molecular weight of imipramine hydrochloride, 316.87
- M_{r2} = molecular weight of imipramine pamoate, 949.18
- D = dilution factor of the *Sample solution*
- V = volume of *Medium 1* or *Medium 2*, 900 mL
- L = label claim (mg/Capsule)

Tolerances: See [Table 2](#).

Table 2

Time Point (i)	Time (min)	Amount Dissolved NLT (%)
1	30	40
2	90	75

The percentage of imipramine pamoate dissolved equivalent to the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2 \cdot HCl$) dissolved at the times specified conforms to [Dissolution \(711\)](#), [Acceptance Table 1](#).

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

Medium: [0.1 N hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm