Propafenone Hydrochloride Extended-Release Capsules

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Expert Committee	Chemical Medicines Monographs 2

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Chemical Medicines Monographs 2 Expert Committee intends to revise the Propafenone Hydrochloride Extended-Release Capsules monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add *Dissolution Test 4* to the monograph.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

The revision also necessitates a change in the table numbering in the tests for *Organic Impurities* and *Content of Propafenone Related Compound A*.

See below for additional information about the proposed text.[1]

Should you have any questions, please contact Donald Min**,** Ph.D., Senior Scientific Liaison to the Chemical Medicines Monographs 2 Expert Committee (301-230-7457 or ddm@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted which will include the changes indicated herein as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program which are posted without prior publication for comment in *Pharmacopeial Forum*, must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF* for Revision Bulletins.

Propafenone Hydrochloride Extended-Release Capsules

DEFINITION

Propafenone Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$).

IDENTIFICATION

- **A. Infrared Absorption ⟨197K⟩**
- **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

- **Procedure**

Buffer: Dissolve 1.36 g/L of monobasic potassium phosphate in water, and adjust with phosphoric acid to a pH of 3.0 ± 0.1.

Mobile phase: Methanol and *Buffer* (50:50)

Diluent: 50% methanol in water

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

Sample stock solution: Nominally 1 mg/mL of propafenone hydrochloride prepared as follows. Transfer a suitable amount of finely powdered contents from NLT 20 Capsules to an appropriate volumetric flask. Add about 60% of the final volume of *Diluent,* and sonicate with occasional swirling until the contents are completely disintegrated. Dilute with *Diluent* to volume and pass through a suitable filter of 0.45-µm pore size.

Sample solution: Nominally 0.1 mg/mL of propafenone hydrochloride in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of propafenone

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 propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution ⟨711⟩**

Test 1

Acid stage

Medium: 0.08 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 1 h

Diluent: 6.8 g/L of monobasic potassium phosphate in water. Adjust with sodium hydroxide to a pH of 6.8.

Standard solution: (L/1000) mg/mL of USP Propafenone Hydrochloride RS in *Diluent*, where L is the label claim in mg/Capsule

Sample solution: At the specified time point, withdraw about 10 mL of the solution and pass through a suitable filter of 0.45-µm pore size. Discard at least the first 4 mL of the filtrate. Analyze the *Sample solution* immediately.

Instrumental conditions

Mode: UV

Analytical wavelengths: 305 and 375 nm

Cell: 0.2 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Measure and subtract the absorbance at 375 nm from the absorbance at 305 nm to obtain the absorbances for the *Sample solution* and *Standard solution*.

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved:

$$\text{Result}_1 = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: See *Table 1*.

Buffer stage

Proceed as directed in the *Acid stage*, except for the following parameters.

Buffer: Dissolve 108.88 g of monobasic potassium phosphate in water, add 14.4 g of sodium hydroxide, mix to dissolve, and dilute with water to 1 L. Adjust with 2 N sodium hydroxide to a pH of 6.8.

Solution A: *Buffer* and 2 N sodium hydroxide (64:36)

Medium: At 2 h of dissolution time, add 100 mL of *Solution A*, preheated at 37°, to 900 mL of 0.08 N hydrochloric acid.

Times: 4 and 12 h

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*

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

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at each time point (*i*):

$$\text{Result}_2 = C_2 \times V \times (1/L) \times 100$$

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

C_i = concentration of propafenone hydrochloride in the portion of sample withdrawn at time point (*i*) (mg/mL)
V = volume of *Medium*, 1000 mL
L = label claim (mg/Capsule)
V_S = volume of *Medium* taken (mL)

Tolerances: See *Table 1*.

Table 1

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	5–25
2	4	40–70
3	12	NLT 75

The percentages of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

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

Acid stage

Acid stage medium: 0.08 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm, with sinkers
Time: 1 h
Standard stock solution: 0.42 mg/mL of USP Propafenone Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Propafenone Hydrochloride RS to a suitable volumetric flask. Add methanol, NMT 10% of the final volume, and sonicate to dissolve. Dilute with *Acid stage medium* to volume.
Standard solution: 0.021 mg/mL of USP Propafenone Hydrochloride RS in *Acid stage medium* from the *Standard stock solution*
Sample solution: Pass the solution through a suitable filter of 0.45-µm pore size. Dilute with *Acid stage medium* to a concentration similar to that of the *Standard solution*.
Instrumental conditions
Mode: UV
Analytical wavelength: 305 nm
Cell: 1 cm
Blank: *Acid stage medium*
Analysis
After 1 h in the *Acid stage medium* and the collection of the *Sample solution*, replace the portion of solution withdrawn with an equal volume of *Acid stage medium*. Continue for an additional 1 h in *Acid stage medium*.
Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved:

$$\text{Result}_1 = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Propafenone Hydrochloride RS in the *Standard solution* (mg/mL)
D = dilution factor (mL/mL)
V = volume of *Acid stage medium*, 900 mL
L = label claim (mg/Capsule)

Tolerances: See *Table 2*.

Buffer stage

Proceed as directed in the *Acid stage*, except for the following parameters.
Buffer stage medium: After 2 h in the *Acid stage*, add 100 mL of phosphate buffer (68 g of monobasic potassium phosphate and 42 g of sodium hydroxide in 1000 mL of water), preheated at 37°, to 900 mL of *Acid stage medium*; 1000 mL.
Times: 6 and 15 h
Standard stock solution: 0.48 mg/mL of USP Propafenone Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Propafenone Hydrochloride RS to a suitable volumetric flask. Add methanol, NMT 10% of the final volume, and sonicate to dissolve. Dilute with *Buffer stage medium* to volume.
Standard solution: 0.048 mg/mL of USP Propafenone Hydrochloride RS in *Buffer stage medium* from *Standard stock solution*
Sample solution: Withdraw a 10-mL aliquot at each time point. Pass the solution through a suitable filter of 0.45-µm pore size. Dilute with *Buffer stage medium* to a concentration similar to that of the *Standard solution*.
Blank: *Buffer stage medium*
Instrumental conditions: See *Acid stage*.
Analysis
At the specified time points, replace the portion of solution withdrawn with 10 mL of *Buffer stage medium*.
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Propafenone Hydrochloride RS in the *Standard solution* (mg/mL)
D = dilution factor (mL/mL)

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at each time point (*i*):

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

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

C_i = concentration of propafenone hydrochloride in the portion of sample withdrawn at time point (*i*) (mg/mL)
V = volume of *Buffer stage medium*, 1000 mL
V_S = volume of the *Sample solution* withdrawn from the *Buffer stage medium* (mL)
L = label claim (mg/Capsule)

Tolerances: See *Table 2*.

Table 2

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	5–25
2	6	45–65
3	15	NLT 80

The percentages of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

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

Acid stage

Acid stage medium: 0.08 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm, with sinkers
Time: 2 h
Phosphate buffer: Dissolve 190.06 g of tribasic sodium phosphate in 1 L of water.
Diluent: *Phosphate buffer* and *Acid stage medium* (12:88). Adjust the pH to 6.8 with phosphoric acid or sodium hydroxide if necessary.
Standard solution: (*L*/1000) mg/mL of USP Propafenone Hydrochloride RS, where *L* is the label claim in mg/Capsule, prepared as follows. Transfer a suitable amount of USP Propafenone Hydrochloride RS to a suitable volumetric flask. Dissolve with 10% of final volume of methanol with aid of sonication. Dilute with *Diluent* to volume.
Sample solution: At the specified time point, withdraw 10 mL of the solution under test and centrifuge. Use the supernatant.
Instrumental conditions
Mode: UV
Analytical wavelengths: 305 nm
Cell: 0.2 cm
Blank: *Diluent*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved:

$$\text{Result}_1 = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Propafenone Hydrochloride RS in the *Standard solution* (mg/mL)
L = label claim (mg/Capsule)
V = volume of *Acid stage medium*, 900 mL

Tolerances: See *Table 3*.

Buffer stage

Proceed as directed in the *Acid stage*, except for the following parameters.
Buffer stage medium: After the samples are withdrawn at 2 h, add 110 mL or appropriate amount of *Phosphate buffer*, preheated at 37°, to *Acid stage medium*, and adjust the pH to 6.8 with phosphoric acid or sodium hydroxide if necessary; 1000 mL.
Times: 4 and 12 h
Sample solution: At the specified time points, withdraw 10 mL of the solution and centrifuge. Use the supernatant.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at each time point (*i*):

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

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

C_i = concentration of propafenone hydrochloride in the portion of sample withdrawn at time point (*i*) (mg/mL)
V = volume of *Buffer stage medium*, 1000 mL
V_S = volume of *Sample solution* withdrawn (mL)
L = label claim (mg/Capsule)

Tolerances: See *Table 3*.

Table 3

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 30
2	4	35–60
3	12	NLT 80

The percentages of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

▲**Test 4:** If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 4*.

Acid stage

Acid stage medium: 0.08 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 2 h
Diluent: Dissolve 6.8 g of monobasic potassium phosphate with 1 L of water. Adjust with sodium hydroxide to a pH of 6.8.

Standard solution: 0.325 mg/mL of USP Propafenone Hydrochloride RS in *Diluent* [NOTE—Sonication may be needed for dissolution.]
Sample solution: At the specified time point, withdraw 5 mL of the solution and pass through a suitable filter. Replace the portion of solution withdrawn with an equal volume of *Medium*.
Instrumental conditions
Mode: UV
Analytical wavelengths: 305 and 375 nm
Cell: 0.2 cm
Blank: *Diluent*
Analysis
Samples: *Standard solution* and *Sample solution*
Measure and subtract the absorbance at 375 nm from the absorbance at 305 nm to obtain the absorbances for the *Sample solution* and *Standard solution*.
Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved:

$$\text{Result}_1 = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Propafenone Hydrochloride RS in the *Standard solution* (mg/mL)
L = label claim (mg/Capsule)
V = volume of *Medium*, 900 mL

Tolerances: See *Table 4*.
Buffer stage
Proceed as directed in the *Acid stage*, except for the following parameters.
Buffer: Dissolve 108.88 g of monobasic potassium phosphate and 14.4 g of sodium hydroxide with 1 L of water. Adjust with 2 N sodium hydroxide to a pH of 6.8.
Solution A: *Buffer* and 2 N sodium hydroxide (64:36)
Medium: At 2 h of dissolution time, add 100 mL of *Solution A*, preheated at 37°, to the vessel containing 900 mL of 0.08 N hydrochloric acid.
Times: 3, 6, and 12 h
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the concentration (C_i) of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at each time point (i):

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$
$$\text{Result}_3 = \{[C_3 \times V] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$
$$\text{Result}_4 = \{[C_4 \times V] + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of propafenone hydrochloride in the portion of sample withdrawn at time point (i) (mg/mL)
V = volume of *Medium*, 1000 mL
V_S = volume of *Medium* taken, 5 mL
L = label claim (mg/Capsule)

Tolerances: See *Table 4*.

Table 4

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	15–35
2	3	26–46
3	6	56–76
4	12	NLT 80

The percentages of the labeled amount of propafenone hydrochloride ($C_{21}H_{27}NO_3 \cdot HCl$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.▲ (TBD)

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Keep all solutions containing propafenone hydrochloride in amber glassware.
Solution A: 0.015 M dibasic potassium phosphate. Adjust with phosphoric acid to a pH of 2.5 ± 0.2.
Solution B: Acetonitrile
Mobile phase: See *Table* ▲*5*.▲ (TBD)

Table ▲**5**▲ (TBD)

Time (min)	Solution A (%)	Solution B (%)
0	65	35
8	65	35
20	30	70
30	30	70
31	65	35
36	65	35

Diluent: 50% methanol in water
System suitability solution: 0.1 mg/mL each of USP Propafenone Hydrochloride RS and USP Propafenone Related Compound B RS in *Diluent*
Standard solution: 2.0 µg/mL of USP Propafenone Hydrochloride RS in *Diluent*. Sonicate if necessary.
Sensitivity solution: 0.3 µg/mL of USP Propafenone Hydrochloride RS in *Diluent* from the *Standard solution*
Sample solution: Nominally 1 mg/mL of propafenone hydrochloride, prepared as follows. Transfer a suitable amount of finely powdered contents from NLT 20 Capsules to an appropriate volumetric flask. Add about 40% of the final volume of *Diluent* and sonicate for about 15 min. Dilute with *Diluent* to volume and pass through a suitable filter of 0.45-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 15-cm; 5-µm packing L7
Column temperature: 30°

Flow rate: 1 mL/min
Injection volume: 20 µL
System suitability
Samples: *System suitability solution*, *Standard solution,* and *Sensitivity solution*
Suitability requirements
Resolution: NLT 3.0 between propafenone related compound B and propafenone, *System suitability solution*
Relative standard deviation: NMT 5.0%, *Standard solution*
Signal-to-noise ratio: NLT 10, *Sensitivity solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each individual unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each unspecified degradation product from the *Sample solution*
r_S = peak response of propafenone from the *Standard solution*
C_S = concentration of USP Propafenone Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of propafenone hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table* ▲6.▲ (TBD) Disregard any peaks below 0.03% (peak area less than that of the *Sensitivity solution*).

Table ▲6▲ (TBD)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Propafenone related compound B[a, b]	0.81	—
Propafenone	1.00	—
Propafenone glycerol analog[a, c]	2.53	—
Flavone[a, d]	2.83	—
Propafenone dimer[a, e]	2.88	—
Propafenone chloroglycerol analog[a, f]	2.91	—
Propafenone glycidyl analog[a, g]	2.96	—
Propafenone phenol[a, h]	3.29	—
Propafenone glycerol dimer[a, i]	3.80	—
Any unspecified degradation product	—	0.15
Total degradation products	—	0.50

[a] Process impurities; do not include in total degradation products.
[b] (*RS*,*E*)-1-{2-[2-Hydroxy-3-(propylamino)propoxy]phenyl}-3-phenylprop-2-en-1-one.
[c] 1-[2-[(2*RS*)-2,3-Dihydroxypropoxy]phenyl]-3-phenylpropan-1-one.
[d] 2-Phenylchroman-4-one.
[e] 1,1′-[Propyliminobis(2-hydroxypropane-3,1-diyl)oxy-2,1-phenylene]bis(3-phenylpropan-1-one).
[f] 1-[2-(3-Chloro-2-hydroxypropoxy)phenyl]-3-phenylpropan-1-one.
[g] 1-[2-[[(*RS*)-Oxiranyl]methoxy]phenyl]-3-phenylpropan-1-one.
[h] 1-(2-Hydroxyphenyl)-3-phenylpropan-1-one.
[i] 1,1′-(2,2′-(2-Hydroxypropane-1,3-diyl)bis(oxy)bis(2,1-phenylene))bis(3-phenylpropan-1-one).

Change to read:

• **CONTENT OF PROPAFENONE RELATED COMPOUND A**
Buffer: Dissolve 3.4 g of dibasic potassium phosphate in 1000 mL of water, and adjust with phosphoric acid to a pH of 2.5 ± 0.05.
Solution A: Methanol and *Buffer* (45:55); pass through a suitable filter of 0.2-µm pore size.
Solution B: Methanol and *Buffer* (75:25); pass through a suitable filter of 0.2-µm pore size.
Mobile phase: See *Table* ▲7.▲ (TBD)

Table ▲7▲ (TBD)

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4.0	100	0
7.0	50	50
10.0	0	100
12.0	0	100
12.5	100	0
15.0	100	0

Diluent: Methanol and water (80:20)
Standard solution: 2.0 µg/mL of USP Propafenone Related Compound A RS in *Diluent*
Sensitivity solution: 0.2 µg/mL of USP Propafenone Related Compound A RS in *Diluent* from the *Standard solution*
Sample solution: Nominally 1 mg/mL of propafenone hydrochloride prepared as follows. Transfer a suitable amount of finely powdered contents from NLT 20 Capsules to an appropriate volumetric flask. Add about 75% of the final volume of *Diluent* and sonicate with intermittent shaking for 20 min. Dilute with *Diluent* to volume and pass through a suitable filter of 0.45-µm pore size. Discard the first 4 mL of the filtrate.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 250 nm
Column: 2.1-mm × 10-cm; 1.7-µm packing L1
Column temperature: 60°
Flow rate: 0.4 mL/min
Injection volume: 4 µL
System suitability
Samples: *Standard solution* and *Sensitivity solution*
Suitability requirements
Tailing factor: NMT 2.0, *Standard solution*
Relative standard deviation: NMT 6.0%, *Standard solution*
Signal-to-noise ratio: NLT 10, *Sensitivity solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of propafenone related compound A in the portion of Capsules taken:

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

r_U = peak response of propafenone related compound A from the *Sample solution*
r_S = peak response of propafenone related compound A from the *Standard solution*
C_S = concentration of USP Propafenone Related Compound A RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: See *Table* ▲*8.*▲ (TBD)

Table ▲**8**▲ (TBD)

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Propafenone	1.0	—
Propafenone related compound A[a]	1.9	0.20

[a] *N*-{2-Hydroxy-3-[2-(3-phenylpropanoyl)phenoxy]propyl}-*N*-propylformamide.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Keep in tight containers and store at controlled room temperature.
- **LABELING:** When more than one test for *Dissolution* is given, the *Labeling* section states the test for *Dissolution* used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS ⟨11⟩**

  USP Propafenone Hydrochloride RS

  USP Propafenone Related Compound A RS
  N-{2-Hydroxy-3-[2-(3-phenylpropanoyl)phenoxy]propyl}-*N*-propylformamide.
  $C_{22}H_{27}NO_4$ 369.45

  USP Propafenone Related Compound B RS
  (*RS*,*E*)-1-{2-[2-Hydroxy-3-(propylamino)propoxy]phenyl}-3-phenylprop-2-en-1-one.
  $C_{21}H_{25}NO_3$ 339.43