

Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Jun-2023
Document Type: USP Monographs
DocId: GUID-8F871A7D-FA33-4C6A-958C-FEB88214B2B1_4_en-US
DOI: https://doi.org/10.31003/USPNF_M5773_04_01
DOI Ref: 06m2s

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Sorafenib Tablets

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DEFINITION
Sorafenib Tablets contain an amount of Sorafenib Tosylate equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of sorafenib ($C_{21}H_{16}ClF_3N_4O_3$).

- 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.
 - **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

- ASSAY**
- **PROCEDURE**
Solution A: 1 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.4.
Solution B: [Alcohol, absolute](#), [acetonitrile](#), and *Solution A* (16:24:60)
Solution C: [Alcohol, absolute](#) and [acetonitrile](#) (40:60)
Solution D: [Water](#). Adjust with [phosphoric acid](#) to a pH of 2.4.
Mobile phase: See [Table 1](#). Return to original conditions and re-equilibrate the system.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
2	100	0
14	33	67

Diluent: *Solution C* and *Solution D* (75:25)
Standard solution: 0.22 mg/mL of [USP Sorafenib Tosylate RS](#) in *Diluent*. Sonicate to aid the dissolution. [NOTE—It is equivalent to 0.16 mg/mL of sorafenib in *Diluent*.]
Sample stock solution: Nominally equivalent to 4 mg/mL of sorafenib in *Diluent*, prepared as follows. Cut 5 Tablets into small pieces and transfer into a 250-mL volumetric flask. Add 150 mL of *Diluent*, shake for NLT 5 h until completely disintegrated and dispersed, and dilute with *Diluent* to volume. Sonicate for 30 min, and centrifuge a portion of this solution for 5 min or pass a portion of this solution through a polytetrafluoroethylene (PTFE) [or equivalent] filter of 0.45-µm pore size. Use the clear supernatant for the *Sample solution* preparation.
Sample solution: Nominally equivalent to 0.16 mg/mL of sorafenib in *Diluent*, from *Sample stock solution*
Chromatographic system
(See [Chromatography \(621\)](#), [System Suitability](#).)
Mode: LC
Detector: UV 235 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.
Column: 4.6-mm × 10-cm; 3.5-µm packing [L1](#)
Column temperature: 40°
Flow rate: 1.5 mL/min
Injection volume: 10 µL
System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–2.0

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sorafenib ($C_{21}H_{16}ClF_3N_4O_3$) 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 Sorafenib Tosylate RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of sorafenib, 464.83

M_{r2} = molecular weight of sorafenib tosylate, 637.03

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#)

▲Test 1▲ (RB 1-Jun-2023)

Medium: 0.1 N [hydrochloric acid](#) containing 1% [sodium lauryl sulfate](#); 900 mL

Apparatus 2: 100 rpm

Time: 15 min

Determine the percentage of the labeled amount of sorafenib ($C_{21}H_{16}ClF_3N_4O_3$) dissolved by using one of the following procedures.

Chromatographic procedure

Buffer: 1.0 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and Buffer (45:55) for Column A, or [acetonitrile](#) and Buffer (50:50) for Column B

Standard stock solution: 1.54 mg/mL of [USP Sorafenib Tosylate RS](#) in [methanol](#)

Standard solution: 0.3 mg/mL of [USP Sorafenib Tosylate RS](#), prepared as follows. Transfer 20 mL of *Standard stock solution* into a 100-mL volumetric flask and dilute with *Medium* to volume. [NOTE—It is equivalent to 0.22 mg/mL of sorafenib.]

Sample solution: Pass a portion of the solution under test through a filter of 10-μm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

Columns

Column A: 2-mm × 5-cm; 5-μm packing [L1](#)

Column B: 3-mm × 5-cm; 5-μm packing [L1](#)

Column temperature: 40°

Flow rate: 2.5 mL/min for Column A or 3.0 mL/min for Column B

Injection volume: 5 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–2.0

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sorafenib ($C_{21}H_{16}ClF_3N_4O_3$) dissolved:



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