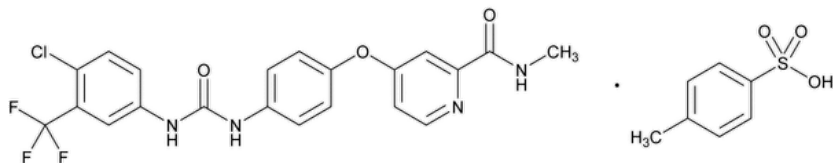


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Add the following:

Sorafenib Tosylate



$C_{21}H_{16}ClF_3N_4O_3 \cdot C_7H_8O_3S$ 637.03
2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, mono(4-methylbenzenesulfonate);
4-(4-{3-[4-Chloro-3-(trifluoromethyl)phenyl]ureido}phenoxy)-N²-methylpyridine-2-carboxamide mono(4-methylbenzenesulfonate) CAS RN[®]:
475207-59-1.
Sorafenib (free base)
 $C_{21}H_{16}ClF_3N_4O_3$ 464.83 CAS RN[®]: 284461-73-0.

DEFINITION
Sorafenib Tosylate contains NLT 97.0% and NMT 102.0% of sorafenib tosylate ($C_{21}H_{16}ClF_3N_4O_3 \cdot C_7H_8O_3S$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#):** [NOTE—Methods described in 197K or 197A may be used.]
- **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**
Protect solutions containing sorafenib tosylate from light. Do not sonicate.
Solution A: 1 mL of [phosphoric acid](#) and 1 g of [potassium phosphate, monobasic](#) in 1 L of [water](#)
Solution B: [Absolute alcohol](#) and [acetonitrile](#) (4:6)
Mobile phase: See [Table 1](#). Return to original conditions, and equilibrate the system for 10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2	95	5
24	56.5	43.5
32	10	90
37	10	90

Diluent: [Dimethyl sulfoxide](#), [acetonitrile](#), and [phosphoric acid](#) (85:15:0.1)
Standard solution: 1.0 mg/mL of [USP Sorafenib Tosylate RS](#) in *Diluent*
Sample solution: 1.0 mg/mL of Sorafenib Tosylate in *Diluent*
Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 2.1-mm × 15-cm; 3.5-μm packing [L7](#)

Column temperature: 75°

Flow rate: 0.6 mL/min

Injection volume: 3 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.6

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sorafenib tosylate ($C_{21}H_{16}ClF_3N_4O_3 \cdot C_7H_8O_3S$) in the portion of Sorafenib Tosylate taken:

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

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 = concentration of Sorafenib Tosylate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• ORGANIC IMPURITIES

Protect solutions containing sorafenib tosylate from light. Do not sonicate.

Solution A, Solution B, Mobile phase, Diluent, Standard solution, and Sample solution: Prepare as directed in the Assay.

System suitability solution: 3.0 μg/mL of [USP Sorafenib Related Compound H RS](#) in *Standard solution*. It contains 3.0 μg/mL of [USP Sorafenib Related Compound H RS](#) and 1.0 mg/mL of [USP Sorafenib Tosylate RS](#) in *Diluent*.

Sensitivity solution: 0.5 μg/mL of [USP Sorafenib Tosylate RS](#) in *Diluent*, from *Standard solution*

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 2.1-mm × 15-cm; 3.5-μm packing [L7](#)

Column temperature: 75°

Flow rate: 0.6 mL/min

Injection volume: 3 μL

System suitability

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

Suitability requirements

Resolution: NLT 2.2 between the sorafenib related compound H and sorafenib peaks, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Sorafenib Tosylate taken:

$$\text{Result} = [r_U \times (1/F)] / \{\Sigma[r_U \times (1/F)] + r_S\} \times 100$$

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

F = relative response factor (see [Table 2](#))