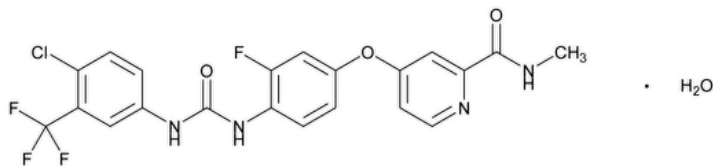


Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-B59A29F2-7A65-48AF-94E8-71AB23F8CD61_2_en-US
DOI: https://doi.org/10.31003/USPNF_M7840_02_01
DOI Ref: s4c5r

© 2025 USPC
Do not distribute

Add the following:

▲Regorafenib



$C_{21}H_{15}ClF_4N_4O_3 \cdot H_2O$ 500.83
2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-fluorophenoxy]-N-methyl-, monohydrate;
4-[4-({[4-Chloro-3-(trifluoromethyl)phenyl]carbamoyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide monohydrate CAS RN®: 1019206-88-2.
Anhydrous
 $C_{21}H_{15}ClF_4N_4O_3$ 482.82 CAS RN®: 755037-03-7.

DEFINITION

Regorafenib contains NLT 97.5% and NMT 101.5% of regorafenib ($C_{21}H_{15}ClF_4N_4O_3$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K or 197A
- **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

Store the solutions containing regorafenib at 2°–8° and protect from light.

Solution A: 0.1% (v/v) [trifluoroacetic acid](#) in [water](#)

Solution B: [Acetonitrile](#) and *Solution A* (3:97)

Mobile phase: See [Table 1](#). Return to original conditions, and equilibrate the system for at least 5 min.

Table 1

Time (min)	Solution B (%)	Acetonitrile (%)
0	100	0
2	100	0
15	78	22
25	60	40
33	36	64
37	36	64

Standard solution: 0.45 mg/mL of [USP Regorafenib RS](#) in [methanol](#)

Sample solution: 0.45 mg/mL of Regorafenib in [methanol](#)

Chromatographic system(See [Chromatography \(621\)](#), [System Suitability](#).)**Mode:** LC**Detector:** UV 232 nm**Column:** 2.1-mm × 15-cm; 3.5-μm packing [L11](#)**Temperatures****Autosampler:** 8°**Column:** 63°**Flow rate:** 0.9 mL/min**Injection volume:** 5 μL**System suitability****Sample:** *Standard solution***Suitability requirements****Tailing factor:** NMT 1.5**Relative standard deviation:** NMT 1.0%**Analysis****Samples:** *Standard solution* and *Sample solution*Calculate the percentage of regorafenib ($C_{21}H_{15}ClF_4N_4O_3$) in the portion of Regorafenib taken:

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

 r_U = peak response of regorafenib from the *Sample solution* r_S = peak response of regorafenib from the *Standard solution* C_S = concentration of [USP Regorafenib RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Regorafenib in the *Sample solution* (mg/mL)**Acceptance criteria:** 97.5%–101.5% on the anhydrous and solvent-free basis**IMPURITIES****• ORGANIC IMPURITIES**

Store the solutions containing regorafenib at 2°–8° and protect from light.

Solution A, Solution B, Mobile phase, and Chromatographic system: Proceed as directed in the Assay.**Standard stock solution:** 1.5 mg/mL of [USP Regorafenib RS](#) in [methanol](#)**Standard solution:** 1.5 μg/mL of [USP Regorafenib RS](#) in [methanol](#), from *Standard stock solution***System suitability solution:** 4.0 μg/mL of [USP Sorafenib Tosylate RS](#) in *Standard stock solution***Sensitivity solution:** 0.75 μg/mL of [USP Regorafenib RS](#) in [methanol](#), from *Standard solution***Sample solution:** 1.5 mg/mL of Regorafenib in [methanol](#)**System suitability****Samples:** *Standard solution*, *System suitability solution*, and *Sensitivity solution*

[NOTE—The relative retention times for sorafenib and regorafenib are 0.9 and 1.0, respectively.]

Suitability requirements**Resolution:** NLT 3.0 between the sorafenib and regorafenib peaks, *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 impurity in the portion of Regorafenib taken:

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

 r_U = peak response of each impurity from the *Sample solution* r_S = peak response of regorafenib from the *Standard solution* C_S = concentration of [USP Regorafenib RS](#) in the *Standard solution* (mg/mL)