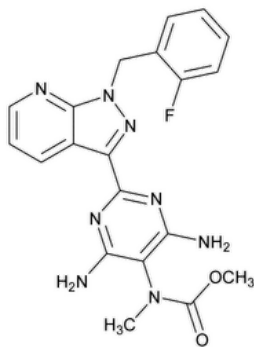


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Add the following:

▲Riociguat



$C_{20}H_{19}FN_8O_2$ 422.42
Carbamic acid, *N*-[4,6-diamino-2-[1-[(2-fluorophenyl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl]-5-pyrimidinyl]-*N*-methyl-, methyl ester;
Methyl *N*-(4,6-diamino-2-[1-[(2-fluorophenyl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl]pyrimidin-5-yl)-*N*-methylcarbamate;
Methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl]pyrimidin-5-yl}(methyl)carbamate CAS RN®: 625115-55-1; UNII: RU3FE2Y4XI.

DEFINITION
Riociguat contains NLT 98.0% and NMT 102.0% of riociguat ($C_{20}H_{19}FN_8O_2$), calculated on the solvent-free basis.

- IDENTIFICATION**
- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197A or 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**

[NOTE—Protect all solutions containing riociguat from light.]

Solution A: [Perchloric acid](#) in [water](#) (4:1000)

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#). Return to the original conditions, and re-equilibrate the system.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
2	75	25
27	65	35
42	32	68
43	10	

Time (min)	Solution A (%)	Solution B (%)
52	10	90

Diluent: *Solution A and Solution B (20:80)*

System suitability solution: 0.4 mg/mL of [USP Riociguat System Suitability Mixture RS](#) in *Diluent*. Sonicate to dissolve as needed.

Standard solution: 0.4 mg/mL of [USP Riociguat RS](#) in *Diluent*. Sonicate to dissolve as needed.

Sample solution: 0.4 mg/mL of Riociguat in *Diluent*. Sonicate to dissolve as needed.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Temperatures

Autosampler: 15°

Column: 40°

Flow rate: 1.0 mL/min

Injection volume: 5 μL

System suitability

Samples: *Standard solution and System suitability solution*

[NOTE—See [Table 2](#) for relative retention times. The relative retention times for riociguat related compound B and riociguat are 0.97 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between riociguat related compound B and riociguat, *System suitability solution*

Tailing factor: 1.0–1.5, *Standard solution*

Relative standard deviation: NMT 0.85% from 6 replicate injections, *Standard solution*

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of riociguat ($C_{20}H_{19}FN_8O_2$) in the portion of Riociguat taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the solvent-free basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **ORGANIC IMPURITIES**

[NOTE—Protect all solutions containing riociguat from light.]

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

Standard solution: 0.0004 mg/mL of [USP Riociguat RS](#) in *Diluent*. Sonicate to dissolve as needed.

Sensitivity solution: 0.0002 mg/mL of [USP Riociguat RS](#) in *Diluent* from *Standard solution*

System suitability

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

[NOTE—See [Table 2](#) for relative retention times. The relative retention times for riociguat related compound B and riociguat are 0.97 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between riociguat related compound B and riociguat, *System suitability solution*



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