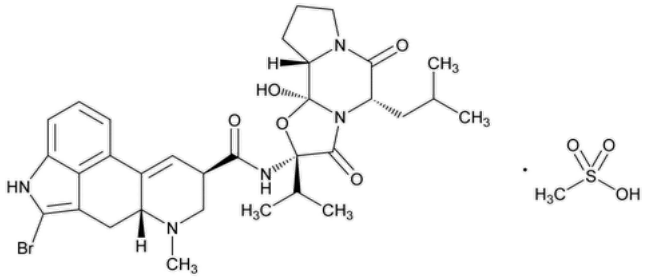
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-C806D49F-5713-46D7-94CB-DA6393D9F963_4_en-US
DOI: https://doi.org/10.31003/USPNF_M10230_04_01
DOI Ref: 46ua4

Bromocriptine Mesylate



$C_{32}H_{40}BrN_5O_5 \cdot CH_4SO_3$ 750.70

Ergotaman-3',6',18-trione, 2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'-(2-methylpropyl)-, monomethanesulfonate (salt), (5'α)-;

2-Bromoergocryptine monomethanesulfonate (salt) CAS RN®: 22260-51-1; UNII: FFP983J3OD.

DEFINITION

Bromocriptine Mesylate contains NLT 98.0% and NMT 102.0% of $C_{32}H_{40}BrN_5O_5 \cdot CH_4SO_3$, calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197M**▲ (CN 1-May-2020) **:** Undried

Change to read:

• **B.** ▲Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: **197U**▲ (CN 1-May-2020)

Sample solution: 50 µg/mL in 0.1 M methanolic methanesulfonic acid

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Sample solution: 600 mg of Bromocriptine Mesylate

Analysis: Dissolve with 80 mL of a mixture of acetic anhydride and glacial acetic acid (7:1). Titrate with 0.1 N perchloric acid VS. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 75.07 mg of $C_{32}H_{40}BrN_5O_5 \cdot CH_4SO_3$.

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Inorganic Impurities

• Residue on Ignition ⟨281⟩**:** NMT 0.1%

Organic Impurities

• **Procedure 1: Limit of Methanesulfonic Acid Content**

Sample solution: 400 mg of Bromocriptine Mesylate

Analysis: Dissolve with 70 mL of methanol. Titrate under nitrogen with 0.1 N methanolic potassium hydroxide VS. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N methanolic potassium hydroxide is equivalent to 9.61 mg of CH_3SO_3H.

Acceptance criteria: NLT 12.5% and NMT 13.4% of CH_3SO_3H on the dried basis

• **Procedure 2**

Solution A: 0.1 N citric acid solution. Adjust with hydrochloric acid to a pH of 2.0.

Diluent: Methanol and *Solution A* (1:1)

Solution B: Acetonitrile and 0.01 M phosphate buffer, pH 7.0 (2:3)

Solution C: Acetonitrile and 0.01 M phosphate buffer, pH 7.0 (3:2)

Mobile phase: See the gradient table below.

Time (min)	Solution B (%)	Solution C (%)
0	100	0
18	100	0
30	0	100
40	0	100
41	100	0

System suitability solution: 2.0 mg/mL each of α-ergocryptine and Bromocriptine Mesylate in *Diluent*

Standard stock solution: 46 µg/mL of USP Bromocriptine Mesylate RS in methanol and *Solution A* (1:1). [NOTE—Dissolve in 50% of the flask volume of methanol and dilute with *Solution A* to volume.]

Standard solution: 4.6 µg/mL of USP Bromocriptine Mesylate RS in *Diluent* from the *Standard stock solution*

Sample solution: 4.6 mg/mL of Bromocriptine Mesylate in methanol and *Solution A* (1:1). [NOTE—Dissolve in 50% of the flask volume of methanol and dilute with *Solution A* to volume.]

Chromatographic system

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

Mode: LC

Detector: UV 300 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

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

[NOTE—The relative retention times for α-ergocryptine and bromocriptine mesylate are 0.46 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 15 between α-ergocryptine and bromocriptine mesylate, *System suitability solution*

Tailing factor: NMT 1.5, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—The relative retention times for bromocriptine and bromocriptinine are 1.0 and 1.7, respectively.]

Calculate the percentage of each impurity in the portion of Bromocriptine Mesylate 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 bromocriptine from the *Standard solution*

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

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

F = relative response factor equal to 1.4 for any peak eluting at a relative retention time of about 0.9 or less, and equal to 1.0 for all other peaks

Acceptance criteria

Individual impurities: NMT 0.4% of bromocriptinine is found; NMT 0.1% of any individual impurity is found.

Total impurities: NMT 1.0%

SPECIFIC TESTS

- **COLOR OF SOLUTION ⟨631⟩**

Matching solutions: Prepare three solutions, A, B, and C, containing, respectively, the following parts of cobaltous chloride CS, ferric chloride CS, cupric sulfate CS, and dilute hydrochloric acid (1 in 40).

A: 3.0:3.0:2.4:31.6

B: 1.0:2.4:0.4:36.2

C: 0.6:2.4:0:37.0

Sample solution: 10 mg/mL of Bromocriptine Mesylate in methanol

Analysis: Compare the *Sample solution* with 10-mL portions of the *Matching solutions* in suitable matched tubes.

Acceptance criteria: The solution is clear and not darker in color than *Matching solutions A*, *B*, and *C*.

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩

Sample solution: 10 mg/mL, in a mixture of methylene chloride and methanol (1:1)

Acceptance criteria: +95° to +105°

- **Loss on Drying**

(See *Thermal Analysis* ⟨891⟩.)

Analysis: Determine the percentage of volatile substances by thermogravimetric analysis using 10 mg of Bromocriptine Mesylate. Heat the specimen under test at the rate of 10°/min in an atmosphere of nitrogen at a flow rate of 45 mL/min. Record the thermogram from ambient temperature to 160°.

Acceptance criteria: It loses NMT 4.0% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, in a cold place.
- **USP Reference Standards** ⟨11⟩

USP Bromocriptine Mesylate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
BROMOCRIPTINE MESYLATE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 36(5)

Current DocID: GUID-C806D49F-5713-46D7-94CB-DA6393D9F963_4_en-US

DOI: https://doi.org/10.31003/USPNF_M10230_04_01

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