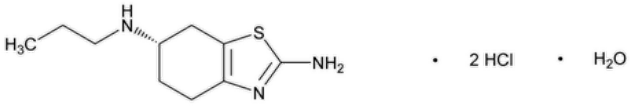
https://trungtamthuoc.com/

Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Dec-2022
Document Type: USP Monographs
DocId: GUID-8F1C63DC-DE51-4104-9869-4D463A4E0B84_5_en-US
DOI: https://doi.org/10.31003/USPNF_M68280_05_01
DOI Ref: m0hmr

© 2025 USPC
Do not distribute

Pramipexole Dihydrochloride



$C_{10}H_{17}N_3S \cdot 2HCl \cdot H_2O$ 302.26

Benzothiazole-2,6-diamine, 4,5,6,7-tetrahydro-N^6-propyl-, dihydrochloride, monohydrate, (*S*)-;

(*S*)-2-Amino-4,5,6,7-tetrahydro-6-(propylamino)benzothiazole dihydrochloride monohydrate CAS RN®: 191217-81-9; UNII: 3D867NP06J.

Change to read:

DEFINITION

Pramipexole Dihydrochloride is a monohydrate and contains NLT 98.0% and NMT 102.0% of pramipexole dihydrochloride (▲$C_{10}H_{17}N_3S \cdot 2HCl$▲ (USP 1-Dec-2022)), calculated on the anhydrous basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197M

Wavelength ranges

For 197A: 3800 cm^{-1} to 650 cm^{-1}

For 197M: 4000 cm^{-1} to 600 cm^{-1}

Acceptance criteria: Meets the requirements

• **B.** The retention time of the major peak of the *Sample solution* corresponds to the pramipexole (*S*-enantiomer) peak of the *System suitability solution* in the test for *Limit of Pramipexole Related Compound D*.

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Sample: 1 mg/mL of Pramipexole Dihydrochloride in water

Acceptance criteria: Meets the requirements of test *A*

ASSAY

Change to read:

• **Procedure**

Solution A: Dissolve 9.1 g of potassium dihydrogen phosphate and 5.0 g of sodium 1-octanesulfonate monohydrate in 1 L of water. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile and *Solution A* (50:50)

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

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
15	20	80
15.1	60	40

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

Time (min)	Solution A (%)	Solution B (%)
20	60	40

System suitability solution: 1.5 mg/mL of USP Pramipexole Dihydrochloride RS and 0.8 mg/mL of USP Pramipexole Related Compound A RS in *Diluent*

Standard solution: 1.5 mg/mL of USP Pramipexole Dihydrochloride RS in *Diluent*

Sample solution: 1.5 mg/mL of Pramipexole Dihydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 264 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40 ± 5°

Flow rate: 1.5 mL/min

Injection volume: 5 µL

System suitability

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

[NOTE—The relative retention times for pramipexole related compound A and pramipexole are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 6.0 between pramipexole related compound A and pramipexole, *System suitability solution*

Tailing factor: NMT 2.0 for pramipexole, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pramipexole dihydrochloride (▲$C_{10}H_{17}N_3S \cdot 2HCl$▲ (USP 1-Dec-2022)) in the portion of Pramipexole Dihydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

C_U = concentration of Pramipexole Dihydrochloride (as monohydrate) in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of pramipexole dihydrochloride, 284.24

M_{r2} = molecular weight of pramipexole dihydrochloride monohydrate, 302.26

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

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.10%

Change to read:

• **LIMIT OF PRAMIPEXOLE RELATED COMPOUND D**

Mobile phase: *n*-Hexane, dehydrated alcohol, and diethylamine (850:150:1)

System suitability stock solution: 1 mg/mL ▲▲ (USP 1-Dec-2022) of USP Pramipexole Dihydrochloride RS and ▲1.3 mg/mL of▲ (USP 1-Dec-2022) USP Pramipexole Related Compound D RS in dehydrated alcohol

System suitability solution: 0.01 mg/mL ▲▲ (USP 1-Dec-2022) of USP Pramipexole Dihydrochloride RS and ▲0.013 mg/mL of▲ (USP 1-Dec-2022) USP Pramipexole Related Compound D RS from the *System suitability stock solution* in *Mobile phase*

Standard stock solution: ▲2.7▲ (USP 1-Dec-2022) mg/mL of USP Pramipexole Related Compound D RS in dehydrated alcohol

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

Standard solution: ▲2.0▲ (USP 1-Dec-2022) µg/mL of USP Pramipexole Related Compound D RS in *Mobile phase* from the *Standard stock solution*

Sample solution: 0.3 mg/mL of Pramipexole Dihydrochloride prepared as follows. Transfer a suitable weighed quantity of Pramipexole Dihydrochloride into a suitable flask, dissolve in 25% of the flask volume of dehydrated alcohol, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 10-µm packing L51

Flow rate: 1.5 mL/min

Injection volume: 75 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for pramipexole related compound D (*R*-enantiomer) and pramipexole (*S*-enantiomer) are 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 5.0 between pramipexole related compound D and pramipexole

Tailing factor: NMT 2.4 for pramipexole

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of pramipexole related compound D in the portion of Pramipexole Dihydrochloride taken:

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

r_U = peak response of pramipexole related compound D from the *Sample solution*

r_S = peak response of pramipexole related compound D from the *Standard solution*

C_S = concentration of USP Pramipexole Related Compound D RS in the *Standard solution* (mg/mL)

C_U = concentration of Pramipexole Dihydrochloride (as monohydrate) in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 1.0% of pramipexole related compound D

- **ORGANIC IMPURITIES**

Solution A, Solution B, Diluent, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 7.5 µg/mL of USP Pramipexole Dihydrochloride RS and 3 µg/mL of USP Pramipexole Related Compound A RS in *Diluent*

Standard solution: 1.5 µg/mL of USP Pramipexole Dihydrochloride RS in *Diluent*

Sample solution: 1.5 mg/mL of Pramipexole Dihydrochloride in *Diluent*

System suitability

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

[NOTE—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 6.0 between pramipexole related compound A and pramipexole, *System suitability solution*

Tailing factor: NMT 2.0 for pramipexole, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Pramipexole Dihydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

C_U = concentration of Pramipexole Dihydrochloride (as monohydrate) in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

M_{r1} = molecular weight of pramipexole dihydrochloride, 284.24

M_{r2} = molecular weight of pramipexole dihydrochloride monohydrate, 302.26

Acceptance criteria: See *Table 2*. Disregard any peak less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor[a]	Acceptance Criteria, NMT (%)
Pramipexole propionamide[b]	0.5	1.0	0.15
Pramipexole related compound A	0.7	1.6	0.15
Pramipexole	1.0	—	—
N-Propylpramipexole[c]	1.4	1.0	0.15
Pramipexole dimer[d]	1.7	1.0	0.15
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] Relative response factor is relative to pramipexole dihydrochloride.

[b] (*S*)-*N*-(2-Amino-4,5,6,7-tetrahydrobenzothiazol-6-yl)propionamide.

[c] (*S*)-2,6-Di(propylamino)-4,5,6,7-tetrahydrobenzothiazole.

[d] N^6,$N^{6'}$-[2-Methylpentane-1,3-diyl]bis(4,5,6,7-tetrahydrobenzothiazole-2,6-diamine). This is a dimer of pramipexole (a mixture of four possible isomers).

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NLT 4.5% and NMT 7.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, protected from moisture and light.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Pramipexole Dihydrochloride RS

[Note—Supplied in monohydrate form.]

USP Pramipexole Related Compound A RS

(*S*)-4,5,6,7-Tetrahydrobenzothiazole-2,6-diamine.

$C_7H_{11}N_3S$ 169.25

USP Pramipexole Related Compound D RS

(*R*)-2-Amino-4,5,6,7-tetrahydro-6-(propylamino)benzothiazole ▲dihydrochloride.

$C_{10}H_{17}N_3S \cdot 2HCl$ 284.25▲ (USP 1-Dec-2022)

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

Topic/Question	Contact	Expert Committee
PRAMIPEXOLE DIHYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(1)

Current DocID: GUID-8F1C63DC-DE51-4104-9869-4D463A4E0B84_5_en-US
DOI: https://doi.org/10.31003/USPNF_M68280_05_01
DOI ref: m0hmr

OFFICIAL