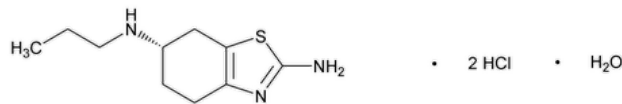


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Pramipexole Dihydrochloride



$\text{C}_{10}\text{H}_{17}\text{N}_3\text{S} \cdot 2\text{HCl} \cdot \text{H}_2\text{O}$ 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.

DEFINITION
Pramipexole Dihydrochloride is a monohydrate and contains NLT 98.0% and NMT 102.0% of pramipexole dihydrochloride ($\text{C}_{10}\text{H}_{17}\text{N}_3\text{S} \cdot 2\text{HCl}$), 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
20	60	40

System suitability solution: 1.5 mg/mL of [USP Pramipexole Dihydrochloride Monohydrate RS](#)▲ (ERR 1-Oct-2025) and 0.8 mg/mL of [USP Pramipexole Related Compound A RS](#) in *Diluent*

Standard solution: 1.5 mg/mL of [USP Pramipexole Dihydrochloride Monohydrate RS](#)▲ (ERR 1-Oct-2025) 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 ($C_{10}H_{17}N_3S \cdot 2HCl$) 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 Monohydrate RS▲](#) (ERR 1-Oct-2025) 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 of [▲USP Pramipexole Dihydrochloride Monohydrate RS▲](#) (ERR 1-Oct-2025) and 1.3 mg/mL of [USP Pramipexole Related Compound D RS](#) in [dehydrated alcohol](#)**System suitability solution:** 0.01 mg/mL of [▲USP Pramipexole Dihydrochloride Monohydrate RS▲](#) (ERR 1-Oct-2025) and 0.013 mg/mL of [USP Pramipexole Related Compound D RS](#) from the *System suitability stock solution* in *Mobile phase***Standard stock solution:** 2.7 mg/mL of [USP Pramipexole Related Compound D RS](#) in [dehydrated alcohol](#)**Standard solution:** 2.0 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

Change to read:

• **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 Monohydrate RS](#) (ERR 1-Oct-2025) and 3 µg/mL of [USP Pramipexole Related Compound A RS](#) in *Diluent*

Standard solution: 1.5 µg/mL of [▲USP Pramipexole Dihydrochloride Monohydrate RS](#) (ERR 1-Oct-2025) 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 Monohydrate RS](#) (ERR 1-Oct-2025) in the *Standard solution* (mg/mL)

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

Name	Relative Retention Time	Relative Response Factor ^a	Acceptance Criteria, NMT (%)
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 N⁶,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 Monohydrate RS](#) ▲ (ERR 1-Oct-2025)
[USP Pramipexole Related Compound A RS](#)
(S)-4,5,6,7-Tetrahydrobenzothiazole-2,6-diamine.
C₇H₁₁N₃S 169.25
 - [USP Pramipexole Related Compound D RS](#)
(R)-2-Amino-4,5,6,7-tetrahydro-6-(propylamino)benzothiazole dihydrochloride.
C₁₀H₁₇N₃S · 2HCl ▲284.24 ▲ (ERR 1-Oct-2025)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
PRAMIPEXOLE DIHYDROCHLORIDE	Documentary Standards Support	SM42025 Small Molecules Therapeutic Areas 4
REFERENCE STANDARDS SUPPORT	RS Technical Services RSTECH@usp.org	SM42025 Small Molecules Therapeutic Areas 4

Chromatographic Database Information: [Chromatographic Database](#)

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