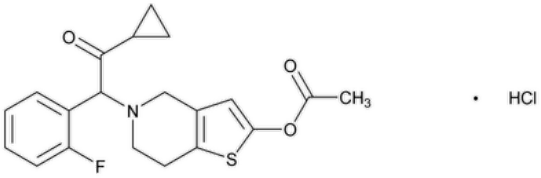
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2023
Document Type: USP Monographs
DocId: GUID-6F4D7843-1F3E-43B5-949B-F88DBD6DFA74_7_en-US
DOI: https://doi.org/10.31003/USPNF_M5157_07_01
DOI Ref: v398p

Prasugrel Hydrochloride

Change to read:



• HCl

$C_{20}H_{20}FNO_3S \cdot HCl$ 409.90

Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4*H*)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, hydrochloride;

5-[2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-yl acetate hydrochloride CAS RN®: 389574-19-0;

▲UNII: ▲G89JQ59I13.

Prasugrel (free base)

$C_{20}H_{20}FNO_3S$ 373.44 CAS RN®: 150322-43-3; UNII: 34K66TBT99.▲ (USP 1-Aug-2023)

DEFINITION

Prasugrel Hydrochloride contains NLT 97.0% and NMT 102.0% of prasugrel hydrochloride ($C_{20}H_{20}FNO_3S \cdot HCl$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

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

Change to read:

• **B.** The retention time of the ▲major▲ (USP 1-Aug-2023) peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

ASSAY

Change to read:

• **Procedure**

Buffer: 10 mM monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.8.

Mobile phase: Acetonitrile and *Buffer* (35:65)

Diluent: Acetonitrile and water (70:30)

Standard solution: 0.1 mg/mL of USP Prasugrel Hydrochloride RS in *Diluent*

Sample solution: 0.1 mg/mL of Prasugrel Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2.5 times the retention time of prasugrel

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0▲▲ (USP 1-Aug-2023)

Relative standard deviation: NMT ▲0.73%▲ (USP 1-Aug-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of prasugrel hydrochloride ($C_{20}H_{20}FNO_3S \cdot HCl$) in the portion of Prasugrel Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 97.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

Delete the following:

▲• **Organic Impurities, Procedure 1**▲ (USP 1-Aug-2023)

Delete the following:

▲• **Organic Impurities, Procedure 2**▲ (USP 1-Aug-2023)

Add the following:

▲• **Organic Impurities**

Buffer: 3 mL of phosphoric acid in 1000 mL of water. Adjust with 10% (w/v) potassium hydroxide solution to a pH of 2.9.

Solution A: *Buffer*

Solution B: Acetonitrile and water (90:10)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	68	32
18	68	32
38	42	58
50	42	58
50.5	68	32
60	68	32

System suitability solution: 1.5 mg/mL of USP Prasugrel Hydrochloride RS and 7.5 µg/mL of USP Prasugrel Related Compound D RS in *Solution B*

Standard solution: 1.5 µg/mL of USP Prasugrel Hydrochloride RS in *Solution B*

Sensitivity solution: 0.75 µg/mL of USP Prasugrel Hydrochloride RS from the *Standard solution* in *Solution B*

Sample solution: 1.5 mg/mL of Prasugrel Hydrochloride in *Solution B*

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

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

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

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

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

Suitability requirements

Resolution: NLT 1.5 between the desacetyl prasugrel diastereomer 1 and desacetyl prasugrel diastereomer 2, *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 specified or any unspecified impurity in the portion of Prasugrel Hydrochloride 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 prasugrel from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Desfluoro prasugrel[a]	0.47	1.0	0.20
Prasugrel acetyl analog[b]	0.53	1.0	0.15
Prasugrel desacetoxy analog[c]	0.61	1.0	0.15
4-Fluoro prasugrel[d]	0.74	1.0	0.15
Desacetyl hydroxyprasugrel[e]	0.86	1.0	0.15
Prasugrel	1.0	—	—
3-Fluoro prasugrel[f]	1.08	1.0	0.30
Prasugrel diketone[g]	1.26	0.67	0.20
Desacetyl prasugrel diastereomer 1[h]	1.33	1.5	0.20
Desacetyl prasugrel diastereomer 2[h]	1.38	1.5	0.50

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Prasugrel chlorobutyryl analog[i]	1.56	0.52	0.30
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 5-(2-Cyclopropyl-2-oxo-1-phenylethyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate.

[b] 5-[1-(2-Fluorophenyl)-2-oxopropyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl)acetate.

[c] 1-Cyclopropyl-2-[6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl]-2-(2-fluorophenyl)ethan-1-one.

[d] 5-[2-Cyclopropyl-1-(4-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate.

[e] 5-[2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-7a-hydroxy-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one.

[f] 5-[2-Cyclopropyl-1-(3-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate.

[g] 1-Cyclopropyl-2-(2-fluorophenyl)ethane-1,2-dione.

[h] 5-[2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one hydrochloride. It is a mixture of diastereomers and shows two peaks in HPLC.

[i] 5-[5-Chloro-1-(2-fluorophenyl)-2-oxopentyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate.

▲ (USP 1-Aug-2023)

SPECIFIC TESTS

Change to read:

• **Water Determination** ⟨921⟩, *Method I*, ▲*Method Ia* ▲*(USP 1-Aug-2023)*, or *Method Ic*: NMT 0.50%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Prasugrel Hydrochloride RS

▲ USP Prasugrel Related Compound D RS

5-[2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one. [Note—This contains desacetyl prasugrel diastereomer 1 and desacetyl prasugrel diastereomer 2 in free base.]

$C_{18}H_{18}FNO_2S$ 331.41▲ (USP 1-Aug-2023)

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

Topic/Question	Contact	Expert Committee
PRASUGREL HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(3)

Current DocID: GUID-6F4D7843-1F3E-43B5-949B-F88DBD6DFA74_7_en-US

DOI: https://doi.org/10.31003/USPNF_M5157_07_01

DOI ref: v398p