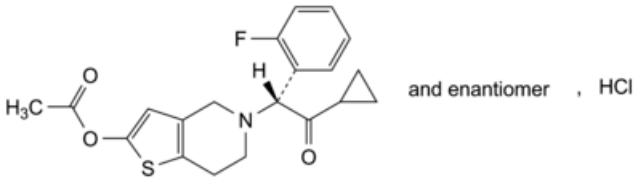
Edition: BP 2025 (Ph. Eur. 11.6 update)

Prasugrel Hydrochloride

General Notices

(Ph. Eur. monograph 3040)



$C_{20}H_{21}ClFNO_3S$ 409.9 *389574-19-0*

Action and use

Inhibitor of ADP-mediated platelet aggregation.

Ph Eur

DEFINITION

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

Content

97.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, slightly hygroscopic powder.

Solubility

Slightly soluble in water, freely soluble in methanol, slightly soluble in acetonitrile, practically insoluble in heptane.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *prasugrel hydrochloride CRS*.

B. It gives reaction (a) of chlorides (2.3.1).

TESTS

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Solvent mixture water R, acetonitrile R (30:70 *V/V*).

Test solution (a) Dissolve 25.0 mg of the substance to be examined in the solvent mixture and dilute to 20.0 mL with the solvent mixture.

Test solution (b) Dilute 2.0 mL of test solution (a) to 25.0 mL with the solvent mixture.

Reference solution (a) Dissolve 25.0 mg of prasugrel hydrochloride CRS in the solvent mixture and dilute to 20.0 mL with the solvent mixture. Dilute 2.0 mL of the solution to 25.0 mL with the solvent mixture.

Reference solution (b) Dilute 1.0 mL of test solution (a) to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (c) Dissolve 2.5 mg of prasugrel for system suitability CRS (containing impurities B and E) in the solvent mixture and dilute to 2 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, *Ø* = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 45 °C.

Mobile phase Mix 35 volumes of acetonitrile R1 and 65 volumes of a 1.36 g/L solution of potassium dihydrogen phosphate R previously adjusted to pH 2.8 with phosphoric acid R.

Flow rate 1.2 mL/min.

Detection Spectrophotometer at 210 nm.

Autosampler Set at 5 °C.

Injection 10 µL of test solution (a) and reference solutions (b) and (c).

Run time 3.6 times the retention time of prasugrel.

Identification of impurities Use the chromatogram supplied with prasugrel for system suitability CRS and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities B and E.

Relative retention With reference to prasugrel (retention time = about 11 min): impurity B = about 1.1; impurity E = about 2.3.

System suitability Reference solution (c):

— resolution: minimum 1.5 between the peaks due to prasugrel and impurity B.

Calculation of percentage contents:

— for each impurity, use the concentration of prasugrel hydrochloride in reference solution (b).

Limits:

— *impurity B*: maximum 0.3 per cent;

— *impurity E*: maximum 0.2 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 1.0 per cent;

— *reporting threshold*: 0.05 per cent.

Water (*2.5.32*)

Maximum 0.5 per cent, determined on 0.100 g by direct sample introduction.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Detection Spectrophotometer at 260 nm.

Injection Test solution (b) and reference solution (a).

Calculate the percentage content of $C_{20}H_{21}ClFNO_3S$ taking into account the assigned content of *prasugrel hydrochloride CRS*.

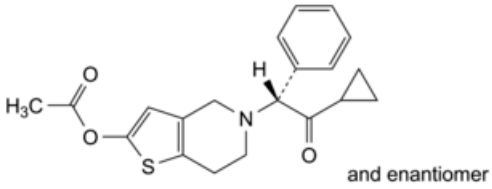
STORAGE

In an airtight container.

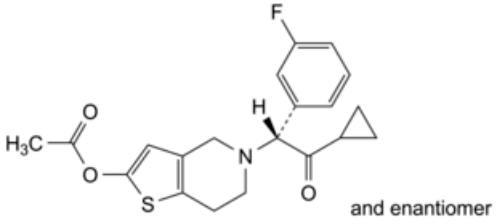
IMPURITIES

Specified impurities *B, E.*

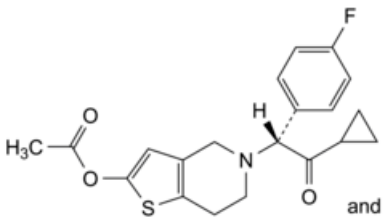
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A, C, D, F, G.*



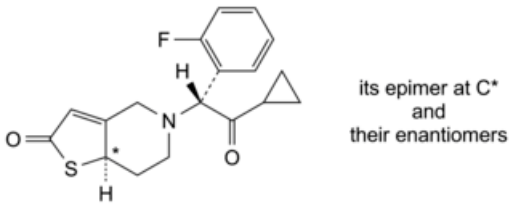
A. 5-[(1*RS*)-2-cyclopropyl-2-oxo-1-phenylethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate,



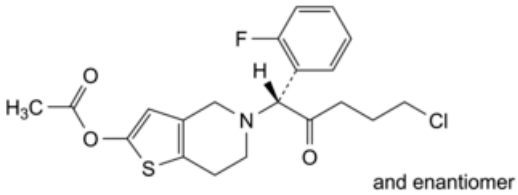
B. 5-[(1*RS*)-2-cyclopropyl-1-(3-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate,



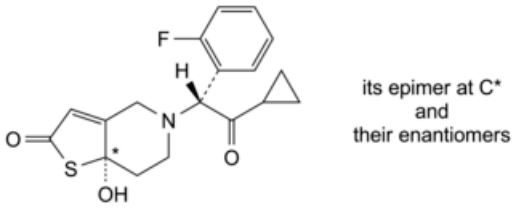
C. 5-[(1*RS*)-2-cyclopropyl-1-(4-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate,



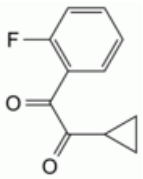
D. mixture of (7a*R*)-5-[(1*RS*)-2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one and (7a*S*)-5-[(1*RS*)-2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one,



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



F. mixture of (7a*R*)-5-[(1*RS*)-2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-7a-hydroxy-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one and (7a*S*)-5-[(1*RS*)-2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-7a-hydroxy-5,6,7,7a-tetrahydrothieno[3,2-*c*]pyridin-2(4*H*)-one,



G. 1-cyclopropyl-2-(2-fluorophenyl)ethane-1,2-dione.
