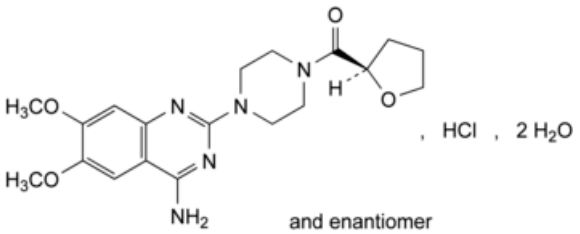
Edition: BP 2025 (Ph. Eur. 11.6 update)

Terazosin Hydrochloride Dihydrate

General Notices

(Ph. Eur. monograph 2021)



$C_{19}H_{26}ClN_5O_4,2H_2O$ 459.9 *70024-40-7*

Action and use

Alpha1-adrenoceptor antagonist.

Ph Eur

DEFINITION

[4-(4-Amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl][(2*RS*)-oxolan-2-yl]methanone hydrochloride dihydrate.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or slightly yellow, crystalline powder.

Solubility

Sparingly soluble in water, slightly soluble in methanol, very slightly soluble in ethanol (96 per cent), practically insoluble in acetone.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison terazosin hydrochloride dihydrate CRS.

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

TESTS

Solution S

Dissolve 1.00 g in carbon dioxide-free water R and dilute to 50.0 mL with the same solvent.

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution Y_7 (2.2.2, Method II).

Dilute 10 mL of solution S to 20 mL with water R.

pH (2.2.3)

3.0 to 5.0 for solution S.

Related substances

Liquid chromatography (2.2.29).

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

Test solution Dissolve 20.0 mg of the substance to be examined in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution 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 (b) Dissolve the contents of a vial of terazosin for system suitability A CRS (containing impurities A, B and C) in 2.5 mL of the solvent mixture.

Reference solution (c) Dissolve 5.0 mg of terazosin impurity N CRS in the solvent mixture and dilute to 100.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 25.0 mL with the solvent mixture.

Reference solution (d) Dissolve 5 mg of terazosin impurity E CRS in the solvent mixture, sonicate for about 5 min and dilute to 100 mL with the solvent mixture. Dilute 1 mL of the solution to 25 mL with the solvent mixture.

Column:

— *size*: *l* = 0.10 m, Ø = 3.0 mm;

— *stationary phase*: end-capped solid core pentafluorophenylpropylsilyl silica gel for chromatography R (2.6 µm).

Mobile phase:

— *mobile phase A*: dilute 1.0 mL of perchloric acid R to 1000 mL with water for chromatography R;

— *mobile phase B*: methanol R1, acetonitrile for chromatography R (10:90 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 1	95	5
1 - 21	95 → 65	5 → 35

Flow rate 0.5 mL/min.

Detection Spectrophotometer at 220 nm.

Injection 0.5 µL.

Identification of impurities Use the chromatogram supplied with *terazosin for system suitability A CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B and C; use the chromatogram obtained with reference solution (d) to identify the peak due to impurity E; use the chromatogram obtained with reference solution (c) to identify the peak due to impurity N.

Relative retention With reference to terazosin (retention time = about 13 min): impurity N = about 0.1; impurity C = about 0.6; impurity A = about 0.78; impurity B = about 0.81; impurity E = about 1.3.

System suitability Reference solution (b):

— *resolution*: minimum 2.0 between the peaks due to impurities A and B.

Calculation of percentage contents:

— *correction factors*: multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.5; impurity C = 0.7;

— for impurity N, use the concentration of the impurity N in reference solution (c);

— for impurities other than N, use the concentration of terazosin hydrochloride dihydrate in reference solution (a).

Limits:

— *impurities A, C, E*: for each impurity, maximum 0.2 per cent;

— *impurity N*: maximum 0.10 per cent;

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

— *total*: maximum 0.5 per cent;

— *reporting threshold*: 0.05 per cent.

Water (*2.5.12*)

7.0 per cent to 8.6 per cent, determined on 0.200 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in a mixture of 5.0 mL of *0.01 M hydrochloric acid* and 50 mL of *methanol R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 42.39 mg of $C_{19}H_{26}ClN_5O_4$.

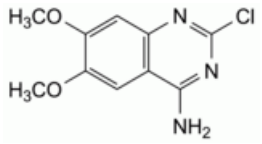
STORAGE

Protected from light.

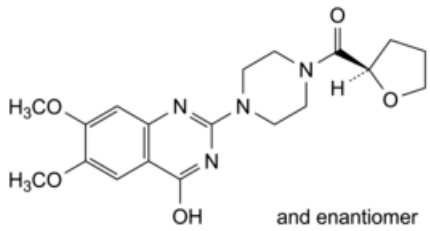
IMPURITIES

Specified impurities *A, C, E, N.*

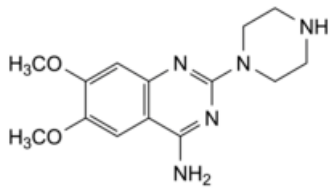
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) *B, D, F, G, H, I, J, K, L, M, O, P.*



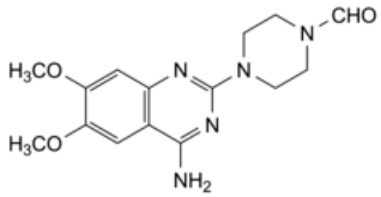
A. 2-chloro-6,7-dimethoxyquinazolin-4-amine,



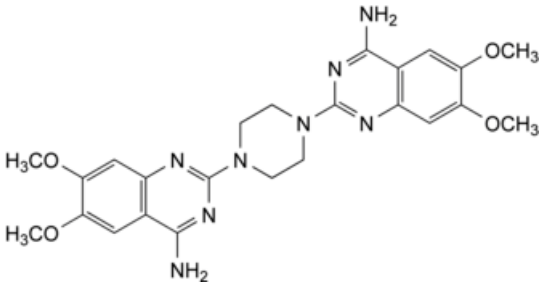
B. [4-(4-hydroxy-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl][(2*RS*)-oxolan-2-yl]methanone,



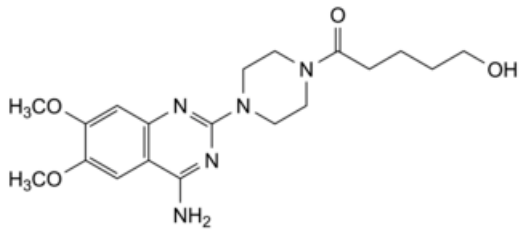
C. 6,7-dimethoxy-2-(piperazin-1-yl)quinazolin-4-amine,



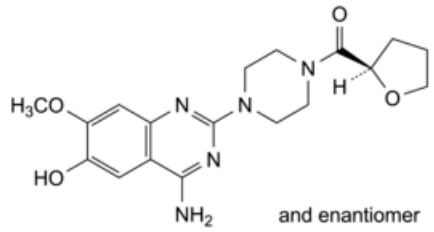
D. [4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl]formaldehyde,



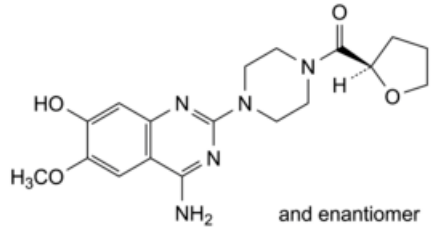
E. 2,2′-(piperazine-1,4-diyl)bis(6,7-dimethoxyquinazolin-4-amine),



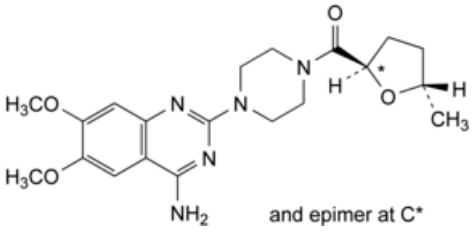
F. 1-[4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl]-5-hydroxypentan-1-one,



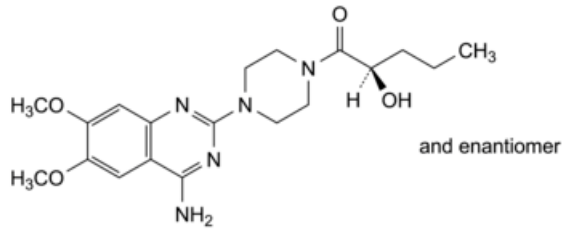
G. [4-(4-amino-6-hydroxy-7-methoxyquinazolin-2-yl)piperazin-1-yl][(2*RS*)-oxolan-2-yl]methanone,



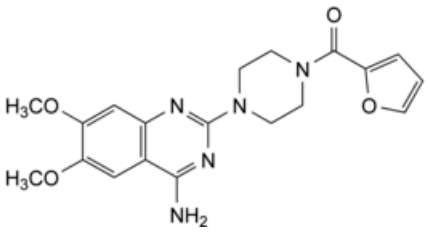
H. [4-(4-amino-7-hydroxy-6-methoxyquinazolin-2-yl)piperazin-1-yl][(2*RS*)-oxolan-2-yl]methanone,



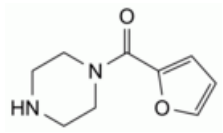
I. [4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl][(2*RS*,5*S*)-5-methyloxolan-2-yl]methanone,



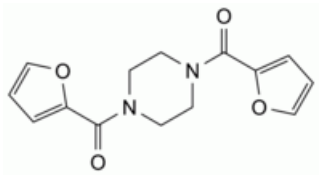
J. (2*RS*)-1-[4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl]-2-hydroxypentan-1-one,



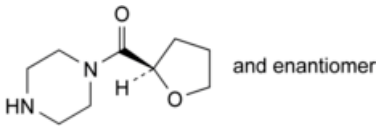
K. [4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl](furan-2-yl)methanone (prazosin),



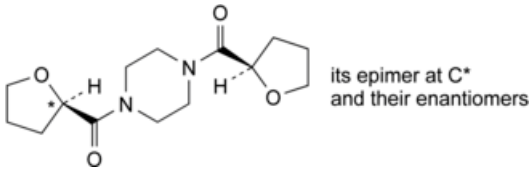
L. (furan-2-yl)(piperazin-1-yl)methanone,



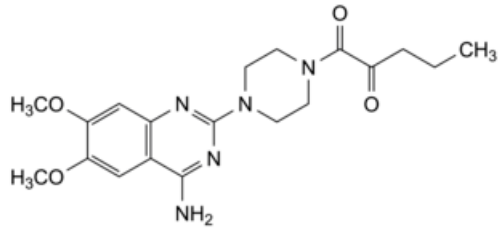
M. (piperazine-1,4-diyl)bis[(furan-2-yl)methanone],



N. [(2*RS*)-oxolan-2-yl](piperazin-1-yl)methanone,



O. mixture of [4-[(2*R*)-oxolane-2-carbonyl]piperazin-1-yl][(2*S*)-oxolan-2-yl]methanone and (piperazine-1,4-diyl)bis[[(2*RS*)-oxolan-2-yl]methanone],



P. 1-[4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl]pentane-1,2-dione.

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