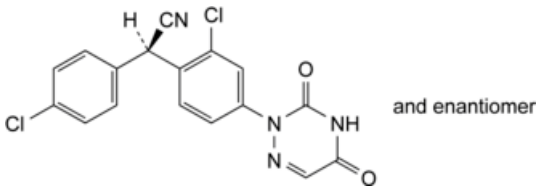
Edition: BP 2025 (Ph. Eur. 11.6 update)

Clazuril

General Notices

(Clazuril for Veterinary Use, Ph. Eur. monograph 1714)



$C_{17}H_{10}Cl_2N_4O_2$ 373.2 *101831-36-1*

Action and use

Treatment of coccidiosis; antiprotozoal (veterinary).

Ph Eur

DEFINITION

(2*RS*)-[2-Chloro-4-(3,5-dioxo-4,5-dihydro-1,2,4-triazin-2(3*H*)-yl)phenyl](4-chlorophenyl)acetonitrile.

Content

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

CHARACTERS

Appearance

White or light yellow powder.

Solubility

Practically insoluble in water, freely soluble in dimethylformamide, slightly soluble in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

A. Melting point (2.2.14): 199 °C to 203 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison clazuril CRS.

TESTS

Related substances

Liquid chromatography (2.2.29).

Solvent mixture tetrahydrofuran R, water R (50:50 *V/V*).

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

Reference solution (a) Dissolve 5 mg of clazuril for system suitability CRS (containing impurities A, B, C, D, E, F, G, H and I) in the solvent mixture and dilute to 5.0 mL with the solvent mixture.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 2.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

— *stationary phase*: octadecylsilyl silica gel for chromatography R (3 µm);

— *temperature*: 35 °C.

Mobile phase:

— *mobile phase A*: mix 100 volumes of a 7.7 g/L solution of ammonium acetate R adjusted to pH 6.2 with a 10 per cent *V/V* solution of anhydrous formic acid R, 150 volumes of acetonitrile R and 750 volumes of water R;

— *mobile phase B*: mix 50 volumes of water R, 100 volumes of a 7.7 g/L solution of ammonium acetate R adjusted to pH 6.2 with a 10 per cent *V/V* solution of anhydrous formic acid R and 850 volumes of acetonitrile R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 20	100 → 0	0 → 100
20 - 25	0	100

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 5 µL.

Identification of impurities Use the chromatogram supplied with clazuril for system suitability CRS and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A, B, C, D, E, F, G, H and I.

Relative retention With reference to clazuril (retention time = about 16 min): impurity A = about 0.6; impurity B = about 0.78; impurity C = about 0.80; impurity D = about 0.86; impurity E = about 0.9; impurity F = about 0.95; impurity G = about 0.98; impurity H = about 1.1; impurity I = about 1.2.

System suitability Reference solution (a):

— peak-to-valley ratio: minimum 1.5, where H_p = height above the baseline of the peak due to impurity G and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to clazuril,

— the chromatogram obtained is similar to the chromatogram supplied with clazuril for system suitability CRS.

Limits:

— *correction factors*: for the calculation of contents, multiply the peak areas of the following impurities by the corresponding correction factor: impurity G = 1.4; impurity H = 0.8;

— *impurities A, B, C, D, E, F, G, H, I*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.20 per cent);

— *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.6 per cent);

— *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard the peaks due to the solvents.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve about 0.260 g in 35 mL of *tetrahydrofuran R* and add 35 mL of *water R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

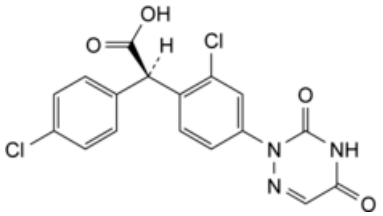
1 mL of *0.1 M sodium hydroxide* is equivalent to 37.32 mg of $C_{17}H_{10}Cl_2N_4O_2$.

STORAGE

Protected from light.

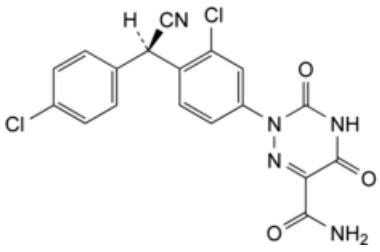
IMPURITIES

Specified impurities *A, B, C, D, E, F, G, H, I.*



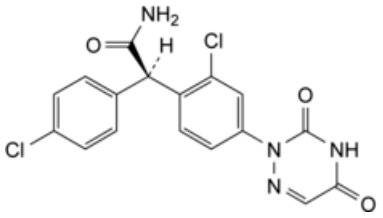
and enantiomer

A. (2*RS*)-[2-chloro-4-(3,5-dioxo-4,5-dihydro-1,2,4-triazin-2(3*H*)-yl)phenyl](4-chlorophenyl)acetic acid,



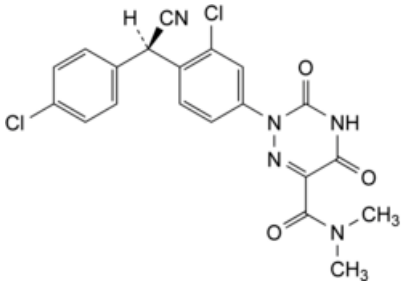
and enantiomer

B. 2-[3-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]phenyl]-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide,



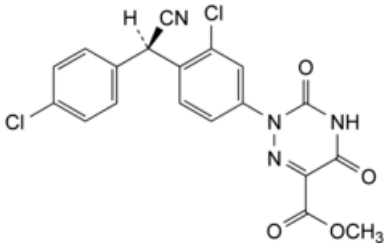
and enantiomer

C. (2*RS*)-2-[2-chloro-4-(3,5-dioxo-4,5-dihydro-1,2,4-triazin-2(3*H*)-yl)phenyl]-2-(4-chlorophenyl)acetamide,



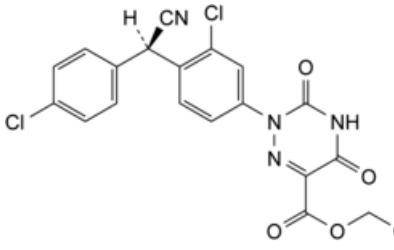
and enantiomer

D. 2-[3-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]phenyl]-*N*,*N*-dimethyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide,



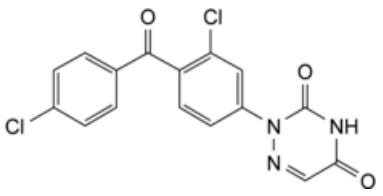
and enantiomer

E. methyl 2-[3-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]phenyl]-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxylate,

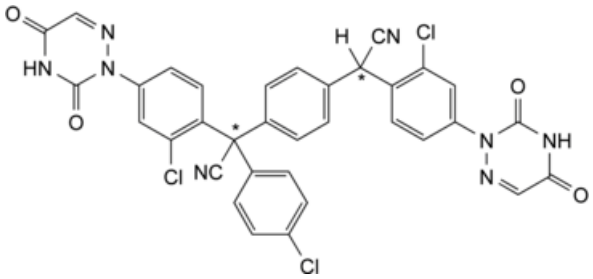


and enantiomer

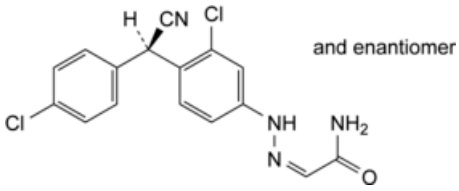
F. ethyl 2-[3-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]phenyl]-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxylate,



G. 2-[3-chloro-4-(4-chlorobenzoyl)phenyl]-1,2,4-triazine3,5(2*H*,4*H*)-dione,



H. [2-chloro-4-(3,5-dioxo-4,5-dihydro-1,2,4-triazin-2(3*H*)-yl)phenyl][4-[[2-chloro-4-(3,5-dioxo-4,5-dihydro-1,2,4-triazin-2(3*H*)-yl)phenyl]cyanomethyl]phenyl](4-chlorophenyl)acetonitrile,



I. (*Z*)-2-[[3-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]phenyl]diazanylidene]acetamide.

Ph Eur