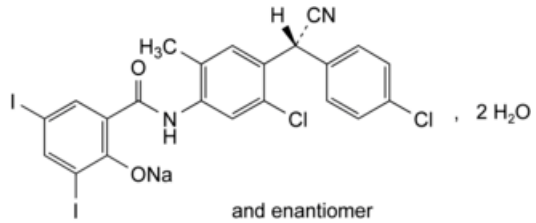
Edition: BP 2025 (Ph. Eur. 11.6 update)

Closantel Sodium Dihydrate

General Notices

(Closantel Sodium Dihydrate for Veterinary Use, Ph. Eur. monograph 1716)



$C_{22}H_{13}Cl_2I_2N_2NaO_2,2H_2O$ 685 (anhydrous substance)

Anhydrous closantel sodium *61438-64-0*

Action and use

Antihelminthic.

Ph Eur

DEFINITION

N-[5-Chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]-2-methylphenyl]-2-hydroxy-3,5-diiodobenzamide sodium salt dihydrate.

Content

98.5 per cent to 101.5 per cent (anhydrous substance).

CHARACTERS

Appearance

Yellow powder, slightly hygroscopic.

Solubility

Very slightly soluble in water, freely soluble in ethanol (96 per cent), soluble in methanol.

It shows polymorphism (*5.9*).

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24), without recrystallisation.

Comparison *closantel sodium dihydrate CRS*.

B. Dissolve 0.1 g in 2 mL of *ethanol (96 per cent) R*. The solution gives reaction (a) of sodium (2.3.1).

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution GY_4 (2.2.2, *Method II*).

Dissolve 0.50 g in *ethanol (96 per cent) R* and dilute to 50 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use and protect from light.*

Test solution Dissolve 0.100 g of the substance to be examined in *methanol R* and dilute to 10.0 mL with the same solvent.

Reference solution (a) Dissolve 10 mg of *closantel for system suitability CRS* (containing impurities A to J) in *methanol R* and dilute to 1.0 mL with the same solvent.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with *methanol R*. Dilute 5.0 mL of this solution to 25.0 mL with *methanol R*.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

— *stationary phase*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (3 µm);

— *temperature*: 35 °C.

Mobile phase:

— *mobile phase A*: to 100 mL of a 7.7 g/L solution of *ammonium acetate R* previously adjusted to pH 4.3 with *acetic acid R*, add 50 mL of *acetonitrile for chromatography R* and 850 mL of *water for chromatography R*;

— *mobile phase B*: to 100 mL of a 7.7 g/L solution of *ammonium acetate R* previously adjusted to pH 4.3 with *acetic acid R*, add 50 mL of *water for chromatography R* and 850 mL of *acetonitrile for chromatography R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	50	50
2 - 22	50 → 20	50 → 80
22 - 27	20	80

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 240 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram supplied with *closantel 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, I and J.

Relative retention With reference to closantel (retention time = about 16 min): impurity A = about 0.07; impurity B = about 0.48; impurity C = about 0.62; impurity D = about 0.65; impurity E = about 0.82; impurity F = about 0.89; impurity G = about 0.93; impurity H = about 1.13; impurity I = about 1.16; impurity J = about 1.55.

System suitability Reference solution (a):

— *resolution*: baseline separation between the peaks due to impurity G and closantel;

— the chromatogram obtained is similar to the chromatogram supplied with *closantel 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 A = 1.5; impurity B = 1.3;

— *impurity G*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *impurities F, H, I*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

— *impurities A, B, C, D, E, J*: 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 7.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 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).

Water (*2.5.12*)

4.8 per cent to 5.8 per cent, determined on 0.250 g.

Use a mixture of 1 volume of *dimethylformamide R* and 4 volumes of *methanol R* as the solvent.

ASSAY

Dissolve 0.500 g in 50 mL of a mixture of 1 volume of *anhydrous acetic acid R* and 7 volumes of *methyl ethyl ketone R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

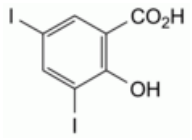
1 mL of *0.1 M perchloric acid* is equivalent to 68.5 mg of $C_{22}H_{13}Cl_2I_2N_2NaO_2$.

STORAGE

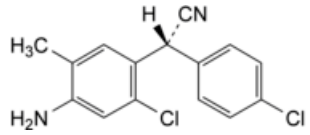
In an airtight container, protected from light.

IMPURITIES

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

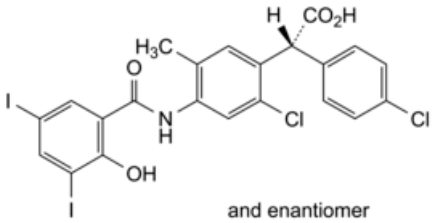


A. 2-hydroxy-3,5-diiodobenzoic acid,



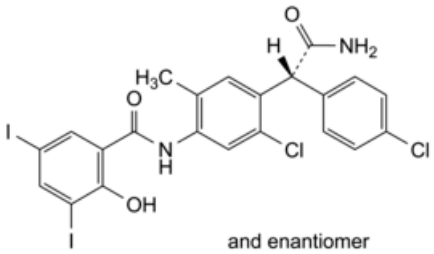
and enantiomer

B. (2*RS*)-(4-amino-2-chloro-5-methylphenyl)(4-chlorophenyl)ethanenitrile,



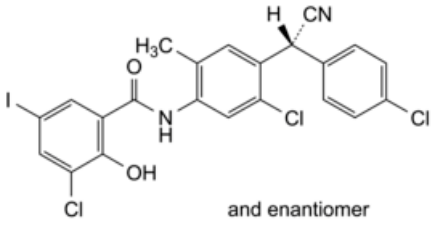
and enantiomer

C. (2*RS*)-[2-chloro-4-[(2-hydroxy-3,5-diiodobenzoyl)amino]-5-methylphenyl](4-chlorophenyl)acetic acid,



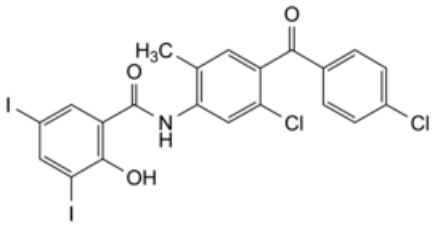
and enantiomer

D. *N*-[4-[(1*RS*)-2-amino-1-(4-chlorophenyl)-2-oxoethyl]-5-chloro-2-methylphenyl]-2-hydroxy-3,5-diiodobenzamide,

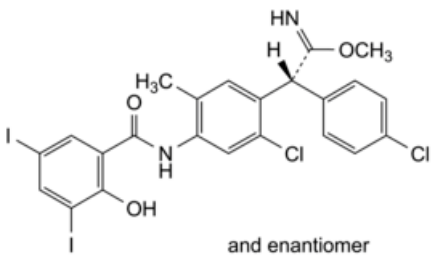


and enantiomer

E. 3-chloro-*N*-[5-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]-2-methylphenyl]-2-hydroxy-5-iodobenzamide,

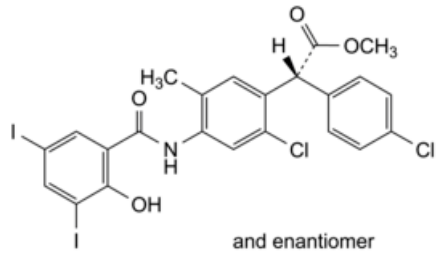


F. *N*-[5-chloro-4-(4-chlorobenzoyl)-2-methylphenyl]-2-hydroxy-3,5-diiodobenzamide,



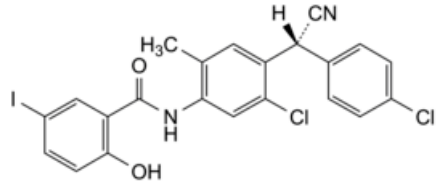
and enantiomer

G. methyl (2*RS*)-2-[2-chloro-4-[(2-hydroxy-3,5-diiodobenzoyl)amino]-5-methylphenyl]-2-(4-chlorophenyl)acetimidate,



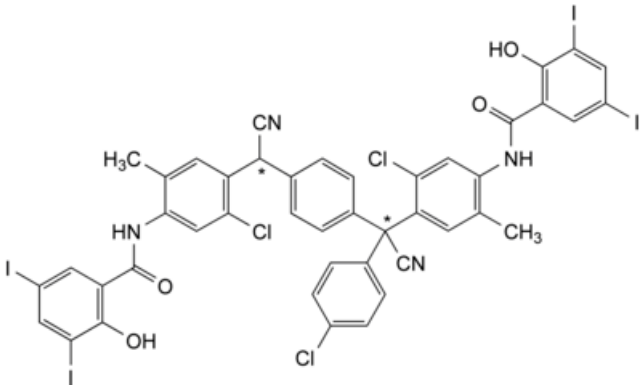
and enantiomer

H. methyl (2*RS*)-[2-chloro-4-[(2-hydroxy-3,5-diiodobenzoyl)amino]-5-methylphenyl](4-chlorophenyl)acetate,



and enantiomer

I. *N*-[5-chloro-4-[(*RS*)-(4-chlorophenyl)cyanomethyl]-2-methylphenyl]-2-hydroxy-5-iodobenzamide,



J. *N*-[5-chloro-4-[[4-[[2-chloro-4-[(2-hydroxy-3,5-diiodobenzoyl)amino]-5-methylphenyl]cyanomethyl]phenyl](4-chlorophenyl)cyanomethyl]-2-methylphenyl]-2-hydroxy-3,5-diiodobenzamide.

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