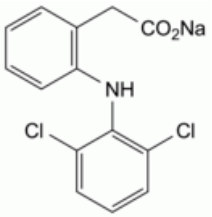
Edition: BP 2025 (Ph. Eur. 11.6 update)

Diclofenac Sodium

General Notices

(Ph. Eur. monograph 1002)



$C_{14}H_{10}Cl_2NNaO_2$ 318.1 *15307-79-6*

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

Preparations

Diclofenac Prolonged-release Capsules

Diclofenac Gastro-resistant Tablets

Diclofenac Prolonged-release Tablets

Ph Eur

DEFINITION

Sodium [2-[(2,6-dichlorophenyl)amino]phenyl]acetate.

Content

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

CHARACTERS

Appearance

White or slightly yellowish, slightly hygroscopic, crystalline powder.

Solubility

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

mp

About 280 °C, with decomposition.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *diclofenac sodium CRS*.

B. Thin-layer chromatography (2.2.27).

Test solution Dissolve 25 mg of the substance to be examined in *methanol R* and dilute to 5 mL with the same solvent.

Reference solution (a) Dissolve 25 mg of *diclofenac sodium CRS* in *methanol R* and dilute to 5 mL with the same solvent.

Reference solution (b) Dissolve 10 mg of *indometacin R* in reference solution (a) and dilute to 2 mL with reference solution (a).

Plate *TLC silica gel GF_{254} plate R*.

Mobile phase *concentrated ammonia R*, *methanol R*, *ethyl acetate R* (10:10:80 *V/V/V*).

Application 5 µL.

Development Over 1/2 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm.

System suitability Reference solution (b):

— the chromatogram shows 2 clearly separated spots.

Results The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

C. Dissolve about 10 mg in 10 mL of *ethanol (96 per cent) R*. To 1 mL of this solution add 0.2 mL of a mixture, prepared immediately before use, of equal volumes of a 6 g/L solution of *potassium ferricyanide R* and a 9 g/L solution of *ferric chloride R*. Allow to stand protected from light for 5 min. Add 3 mL of a 10 g/L solution of *hydrochloric acid R*. Allow to stand, protected from light, for 15 min. A blue colour develops and a precipitate is formed.

D. Dissolve 60 mg in 0.5 mL of *methanol R* and add 0.5 mL of *water R*. The solution gives reaction (b) of sodium (2.3.1).

TESTS

Appearance of solution

The solution is clear (2.2.1) and its absorbance (2.2.25) at 440 nm is not greater than 0.05.

Dissolve 1.25 g in *methanol R* and dilute to 25.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (a) Dilute 2.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b) Dissolve the contents of a vial of *diclofenac for system suitability CRS* (containing impurities A and F) in 1 mL of the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

Mobile phase Mix 34 volumes of a solution containing 0.5 g/L of *phosphoric acid R* and 0.8 g/L of *sodium dihydrogen phosphate R*, previously adjusted to pH 2.5 with *phosphoric acid R*, and 66 volumes of *methanol R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 20 µL.

Run time 1.6 times the retention time of diclofenac.

Identification of impurities Use the chromatogram supplied with *diclofenac for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and F.

Relative retention With reference to diclofenac (retention time = about 25 min): impurity A = about 0.4; impurity F = about 0.8.

System suitability Reference solution (b):

— *resolution*: minimum 4.0 between the peaks due to impurity F and diclofenac.

Calculation of percentage contents:

— *correction factors*: multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.7; impurity F = 0.3;

— for each impurity, use the concentration of diclofenac sodium in reference solution (a).

Limits:

— *impurity A*: maximum 0.2 per cent;

— *impurity F*: maximum 0.15 per cent;

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

— *total*: maximum 0.4 per cent;

— *reporting threshold*: 0.05 per cent.

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 3 h.

ASSAY

Dissolve 0.250 g in 60 mL of *anhydrous acetic acid 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 31.81 mg of $C_{14}H_{10}Cl_2NNaO_2$.

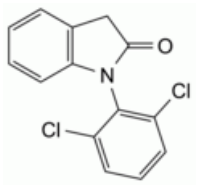
STORAGE

In an airtight container, protected from light.

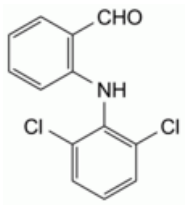
IMPURITIES

Specified impurities A, F.

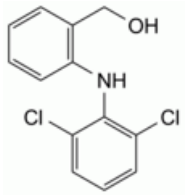
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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, C, D, E.



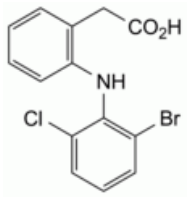
A. 1-(2,6-dichlorophenyl)-1,3-dihydro-2*H*-indol-2-one,



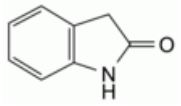
B. 2-[(2,6-dichlorophenyl)amino]benzaldehyde,



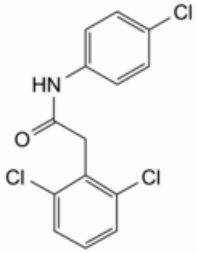
C. [2-[(2,6-dichlorophenyl)amino]phenyl]methanol,



D. [2-[(2-bromo-6-chlorophenyl)amino]phenyl]acetic acid,



E. 1,3-dihydro-2*H*-indol-2-one,



F. *N*-(4-chlorophenyl)-2-(2,6-dichlorophenyl)acetamide.

Ph Eur