Diclofenac Diethylamine

**General Notices**

*Details for the public consultation of this monograph are as follows:*

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<tr>
<th>EAG/Panel/Working Party</th>
<th>Medicinal Chemicals 2</th>
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<td>Deadline for Comment</td>
<td>30th December 2020</td>
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<td>Target Publication Date (subject to change)</td>
<td>BP 2022</td>
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<td>Notes</td>
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<td>If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.</td>
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<td><strong>Related substances</strong> Correction factor has been applied to impurities A and F</td>
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Diclofenac Diethylamine is diethylammonium 2-[(2,6-dichloroanilino)phenyl]acetate. It contains not less than 99.0% and not more than 101.0% of C₁₈H₂₂Cl₂N₂O₂, calculated with reference to the dried substance.

**CHARACTERISTICS**

A white to light beige, crystalline powder.
Sparingly soluble in water and in acetone; freely soluble in ethanol (96%) and in methanol; practically insoluble in 1M sodium hydroxide.

It melts at about 154°, with decomposition.

IDENTIFICATION

A. The infrared absorption spectrum, Appendix II A, is concordant with the reference spectrum of diclofenac diethylamine (RS 371).

B. Carry out the method for thin-layer chromatography, Appendix III A, using the following solutions in methanol.

1. 5.0% w/v of the substance being examined.
2. 5.0% w/v of diclofenac diethylamine BPCRS.

CHROMATOGRAPHIC CONDITIONS

(a) Use a silica gel precoated plate (Macherey Nagel SIL G-25 HR or silica gel 60F254 HPTLC plates are suitable).

(b) Use the mobile phase as described below.

(c) Apply 2 µL of each solution.

(d) Develop the plate to 15 cm.

(e) After removal of the plate, dry it in a stream of warm air for 10 minutes. Spray with ninhydrin solution and heat at 110° for 15 minutes.

MOBILE PHASE

1 volume of hydrochloric acid, 1 volume of water, 6 volumes of glacial acetic acid and 11 volumes of ethyl acetate.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (2) shows two clearly separated spots.

CONFIRMATION

The two principal spots in the chromatogram obtained with solution (1) are similar in position, colour and size to the corresponding spots in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH of a 1% w/v solution in ethanol (10%), 6.4 to 8.4, Appendix V L.

Clarity and colour of solution

A 5% w/v solution in methanol is clear, Appendix IV A. The absorbance of the solution measured at 440 nm is not greater than 0.05, Appendix II B.

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in the mobile phase.

1. 0.10% w/v of the substance being examined.
2. Dilute 2 volumes of solution (1) to 100 volumes and dilute 1 volume of this solution to 10 volumes.
3. Dissolve 1 mg of diclofenac impurity A BPCRS in 1 mL of solution (1) and dilute to 200 mL.

CHROMATOGRAPHIC CONDITIONS
(a) Use a stainless steel column (25 cm × 4.6 mm) packed with end-capped octylsilyl silica gel for chromatography (5 µm) (end-capped Zorbax C8 is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 1 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 254 nm.

(f) Inject 20 µL of each solution.

(g) Allow the chromatography to proceed for 1.5 times the retention time of diclofenac.

**MOBILE PHASE**

34 volumes of a mixture of equal volumes of a 0.1% w/v solution of orthophosphoric acid and a 0.16% w/v solution of sodium dihydrogen orthophosphate adjusted to pH 2.5 and 66 volumes of methanol.

When the chromatograms are recorded under the prescribed conditions, the relative retention times with reference to diclofenac (retention time about 25 minutes) are: impurity A, about 0.4 and impurity F, about 0.8.

**SYSTEM SUITABILITY**

The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between the peaks corresponding to diclofenac and diclofenac impurity A is at least 6.5.

**LIMITS**

Identify the peaks due to impurity A using the chromatogram obtained with solution (3) and multiply the area of the peak by a correction factor of 0.7. Identify the peak due to impurity F using the relative retention time and multiply the area of the peak by a correction factor of 0.3.

In the chromatogram obtained with solution (1):

the area of any secondary peak is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any secondary peaks is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

**Loss on drying**

When dried at a pressure not exceeding 1 kPa for 24 hours, loses not more than 0.5% of its weight. Use 1 g.

**Sulfated ash**

Not more than 0.1%, Appendix IX A, Method II. Use 1 g.

**ASSAY**

Dissolve 0.5 g in 30 mL of anhydrous acetic acid and carry out Method I for non-aqueous titration, Appendix VIII A, determining the end point potentiometrically. Each mL of 0.1M perchloric acid VS is equivalent to 36.93 mg of C_{18}H_{22}Cl_{2}N_{2}O_{2}.
STORAGE

Diclofenac Diethylamine should be kept in an airtight container and protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Diclofenac Sodium.