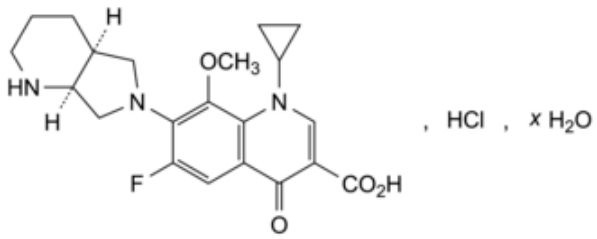
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Moxifloxacin Hydrochloride

General Notices

*(Ph. Eur. monograph 2254)*




$C_{21}H_{25}ClFN_3O_4,xH_2O$ 437.9 (anhydrous substance)

Anhydrous moxifloxacin hydrochloride *186826-86-8*

**Action and use**

Fluoroquinolone antibacterial.

**Preparation**

Moxifloxacin Intracameral Injection

Ph Eur

## DEFINITION

1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.

**Content**

98.0 per cent to 102.0 per cent (anhydrous substance).

It may be anhydrous or contain a variable quantity of water.

## CHARACTERS

### Appearance

Light yellow or yellow powder or crystals.

### Solubility

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

It shows polymorphism (5.9).

## IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

*Comparison* *moxifloxacin hydrochloride CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *anhydrous ethanol R*, evaporate to dryness and record new spectra using the residues.

B. Enantiomeric purity (see Tests).
C. Dissolve 50 mg in 5 mL of *water R*, add 1 mL of *dilute nitric acid R*, mix, allow to stand for 5 min and filter. The filtrate gives reaction (a) of chlorides (2.3.1).

## TESTS

### Appearance of solution

The solution is not more opalescent than reference suspension II (2.2.1) and not more intensely coloured than reference solution $GY_2$ (2.2.2, *Method II*). If intended for use in the manufacture of parenteral preparations, the solution is clear (2.2.1) and not more intensely coloured than reference solution $GY_2$ (2.2.2, *Method II*).

Dissolve 1.0 g in 20 mL of *dilute sodium hydroxide solution R*.

**pH** (2.2.3)

3.9 to 4.6.

Dissolve 0.10 g in 50 mL of *carbon dioxide-free water R*.

### Enantiomeric purity

Liquid chromatography (2.2.29).

*Buffer solution* Dissolve 2.49 g of *anhydrous copper sulfate R* and 2.6 g of *isoleucine R* in 1000 mL of *water for chromatography R*.

*Test solution* Dissolve 5.0 mg of the substance to be examined in *water R* and dilute to 5.0 mL with the same solvent.

*Reference solution (a)* Dilute 3.0 mL of the test solution to 200.0 mL with *water R*. Dilute 1.0 mL of this solution to 10.0 mL with *water R*.

*Reference solution (b)* Dissolve 5 mg of *moxifloxacin for system suitability CRS* (containing impurity G) in 5 mL of *water R*.

*Column*:

— *size*: *l* = 0.25 m, Ø = 4.0 mm;

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

*Mobile phase* *methanol R*, buffer solution (25:75 *V/V*).

*Flow rate* 1.0 mL/min.

*Detection* Spectrophotometer at 293 nm.

*Injection* 20 µL.

*Run time* 1.5 times the retention time of moxifloxacin.

*Identification of impurities* Use the chromatogram supplied with *moxifloxacin for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peak due to impurity G.

*Relative retention* With reference to moxifloxacin (retention time = about 16 min): impurity G = about 0.9.

*System suitability* Reference solution (b):

— *peak-to-valley ratio*: minimum 2.0, 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 moxifloxacin.

*Calculation of percentage content*:

— for impurity G, use the concentration of moxifloxacin hydrochloride in reference solution (a).

*Limit*:

— *impurity G*: maximum 0.15 per cent.

**Related substances**

Liquid chromatography (*2.2.29*). *Carry out the test protected from light.*

*Solution A* Dissolve 0.50 g of *tetrabutylammonium hydrogen sulfate R* and 1.0 g of *potassium dihydrogen phosphate R* in about 500 mL of *water R*. Add 2 mL of *phosphoric acid R* and 0.050 g of *anhydrous sodium sulfite R* and dilute to 1000 mL with *water R*.

*Test solution (a)* Dissolve 50.0 mg of the substance to be examined in solution A and dilute to 50.0 mL with solution A.

*Test solution (b)* Dilute 1.0 mL of test solution (a) to 10.0 mL with solution A.

*Reference solution (a)* Dilute 1.0 mL of test solution (a) to 100.0 mL with solution A. Dilute 1.0 mL of this solution to 10.0 mL with solution A.

*Reference solution (b)* Dissolve 50.0 mg of *moxifloxacin hydrochloride CRS* in solution A and dilute to 50.0 mL with solution A. Dilute 1.0 mL of the solution to 10.0 mL with solution A.

*Reference solution (c)* Dissolve 5 mg of *moxifloxacin for peak identification A CRS* (containing impurities A, B and E) in 5 mL of solution A.

*Reference solution (d)* Dissolve 2 mg of *moxifloxacin for peak identification B CRS* (containing impurity F) in 2 mL of solution A.

*Column*:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *base-deactivated end-capped phenylsilyl silica gel for chromatography R* (5 µm);

— *temperature*: 45 °C.

*Mobile phase* Mix 28 volumes of *methanol R* and 72 volumes of a solution containing 0.5 g/L of *tetrabutylammonium hydrogen sulfate R*, 1.0 g/L of *potassium dihydrogen phosphate R* and 3.4 g/L of *phosphoric acid R*.

*Flow rate* 1.3 mL/min.

*Detection* Spectrophotometer at 293 nm.

*Injection* 10 µL of test solution (a) and reference solutions (a), (c) and (d).

*Run time* 2.5 times the retention time of moxifloxacin.

*Identification of impurities* Use the chromatogram supplied with *moxifloxacin for peak identification A CRS* and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities A, B and E; use the chromatogram supplied with *moxifloxacin for peak identification B CRS* and the chromatogram obtained with reference solution (d) to identify the peak due to impurity F.

*Relative retention* With reference to moxifloxacin (retention time = about 11 min): impurity F = about 0.9; impurity A = about 1.1; impurity B = about 1.3; impurity E = about 1.7.

*System suitability* Reference solution (c):

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

*Limits*:

— *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity B = 1.4; impurity E = 3.5;

— *impurities B, E, F*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

— *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

**Water** (*2.5.12*)

Maximum 4.5 per cent, determined on 0.200 g.

**Sulfated ash** (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

## ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modification.

*Injection* Test solution (b) and reference solution (b).

Calculate the percentage content of $C_{21}H_{25}ClFN_3O_4$ taking into account the assigned content of *moxifloxacin hydrochloride CRS*.

## STORAGE

In an airtight container, protected from light.

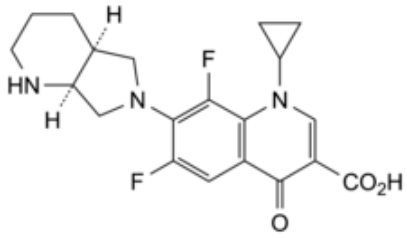
## LABELLING

The label states, where applicable, that the substance is suitable for use in the manufacture of parenteral preparations.

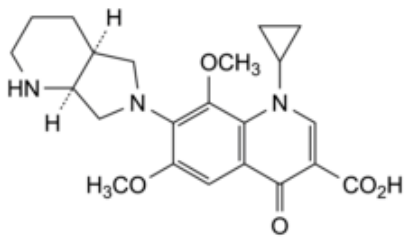
## IMPURITIES

*Specified impurities* *B, E, F, G.*

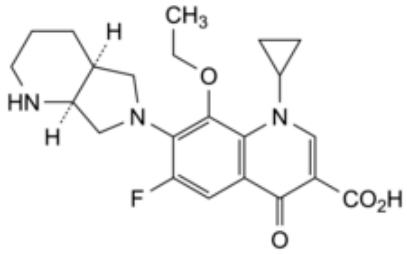
*Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



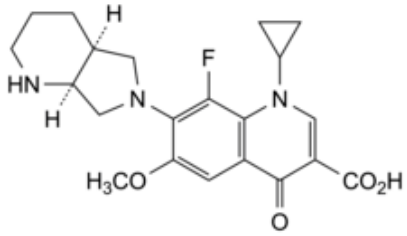

A. 1-cyclopropyl-6,8-difluoro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



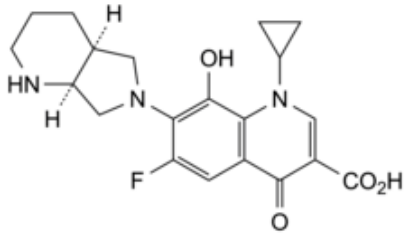
B. 1-cyclopropyl-6,8-dimethoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



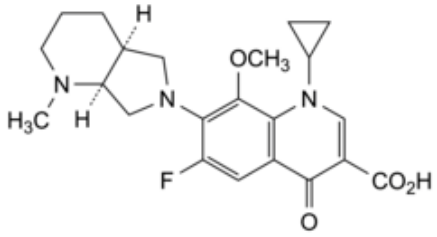
C. 1-cyclopropyl-8-ethoxy-6-fluoro-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



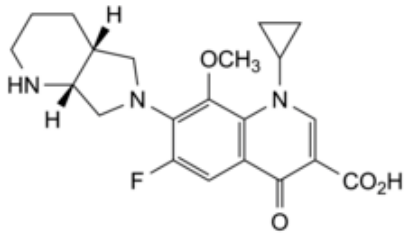
D. 1-cyclopropyl-8-fluoro-6-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



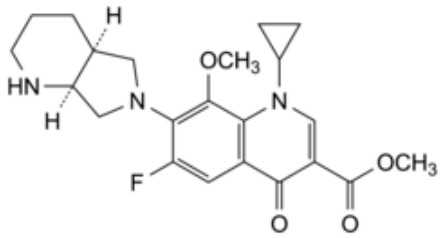
E. 1-cyclopropyl-6-fluoro-8-hydroxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



F. 1-cyclopropyl-6-fluoro-8-methoxy-7-[(4a*S*,7a*S*)-1-methyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



G. 1-cyclopropyl-6-fluoro-8-methoxy-7-[(4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid,



H. methyl 1-cyclopropyl-6-fluoro-8-methoxy-7-[(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylate.

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