



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

Pramipexole Prolonged-release Tablets

General Notices

Prolonged-release Pramipexole Tablets

Pramipexole Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Dopamine receptor agonist; treatment of Parkinson's disease.

DEFINITION

Pramipexole Prolonged-release Tablets contain Pramipexole Dihydrochloride Monohydrate.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of pramipexole. The dissolution profile reflects the *in vivo* performance, which in turn is compatible with the dosage schedule recommended by the manufacturer.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of pramipexole, $C_{10}H_{17}N_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for [thin-layer chromatography](#), [Appendix III A](#), using the following solutions.

(1) Shake a quantity of powdered tablets containing the equivalent of 1 mg of pramipexole in 10 mL of [methanol](#) and filter. Use the filtrate.

(2) 0.01% w/v of [pramipexole BPCRS](#) in [methanol](#).

CHROMATOGRAPHIC CONDITIONS

- (a) Use as the coating [silica gel F₂₅₄](#).
- (b) Use the mobile phase as described below.
- (c) Apply 20 µL of each solution.
- (d) Develop the plate to 15 cm.
- (e) After removal of the plate, dry in air and examine under [ultraviolet light \(254 nm\)](#).

MOBILE PHASE

5 volumes of [methanol](#), 6 volumes of [ammonia](#), 15 volumes of [toluene](#) and 80 volumes of [ethyl acetate](#).

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position, size and colour to that in the chromatogram obtained with solution (2).

B. In the test for Uniformity of content, the chromatogram obtained with solution (1) shows a peak with the same retention time as the peak due to pramipexole in the chromatogram obtained with solution (2).

TESTS

Related substances

Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions.

Solution A 40 volumes of methanol and 60 volumes of mobile phase A.

- (1) Shake a quantity of powdered tablets containing the equivalent of 0.26 mg of pramipexole with 10 mL of solution A. To 4 mL of this solution add sufficient solution A to produce 10 mL and filter.
- (2) Dilute 1 volume of solution (1) to 200 volumes with solution A.
- (3) 0.00375% w/v of [pramipexole for system suitability EPCRS](#) in solution A.
- (4) Dilute 1 volume of solution (2) to 5 volumes with solution A.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Inertsil ODS2 is suitable).
- (b) Use gradient elution and the mobile phase described below.
- (c) Use a flow rate of 1.5 mL per minute.
- (d) Use a column temperature of 40°.
- (e) Use a detection wavelength of 264 nm.
- (f) Inject 200 µL of each solution.

MOBILE PHASE

Mobile phase A Dissolve 5 g of [sodium octanesulfonate monohydrate](#) and 9.1 g of [potassium dihydrogen orthophosphate](#) in 900 mL of [water](#). Adjust to pH 3.0 with [orthophosphoric acid](#) and dilute to 1000 mL with [water](#).

Mobile phase B 50 volumes of [acetonitrile](#) and 50 volumes of mobile phase A.

When the chromatograms are recorded under the prescribed conditions the retention times relative to pramipexole (retention time about 7.24 minutes) are: impurity A, about 0.7; impurity B, about 1.5 and impurity C, about 1.6.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-1	60	40	isocratic
1-16	60→20	40→80	linear gradient
16-20	20	80	isocratic
20-22	20→60	80→40	linear gradient
22-35	60	40	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [resolution](#) between the peaks due to impurity A and pramipexole is at least 6.0.

LIMITS

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) (0.5%);

the sum of the areas of any other [secondary peaks](#) is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (2.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

[Uniformity of content](#)

Tablets containing the equivalent of less than 2 mg and/or less than 2% w/w of pramipexole comply with the requirements stated under [Tablets](#) using the following method of analysis. Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions in solution A, as described under Related substances.

(1) Shake a quantity of powdered tablets containing the equivalent of 0.26 mg of pramipexole with 100mL solution A with the aid of ultrasound. Extract 10 mL, filter and dilute the filtrate, if necessary, to produce a solution containing the equivalent of 0.00013% w/v of pramipexole.

(2) 0.00013% w/v of [pramipexole BPCRS](#).

(3) 0.0003% w/v of [pramipexole BPCRS](#) and 0.0003% w/v of [pramipexole impurity A BPCRS](#).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with [end-capped octadecylsilyl silica gel for chromatography](#) (5 µm) (Inertsil ODS2 is suitable).

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

- (c) Use a flow rate of 1.5 mL per minute.
- (d) Use a column temperature of 40°.
- (e) Use a detection wavelength of 264 nm.
- (f) Inject 200 µL of each solution.

MOBILE PHASE

25 volumes of [acetonitrile](#) and 75 volumes of mobile phase A, as described under Related substances.

When the chromatograms are recorded under the prescribed conditions the retention times for pramipexole and impurity A are about 4 minutes and 3 minutes respectively.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [resolution](#) between the peaks due to impurity A and pramipexole is at least 6.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{10}H_{17}N_3S$ in each tablet using the declared content of $C_{10}H_{17}N_3S$ in [pramipexole BPCRS](#).

ASSAY

For tablets containing the equivalent of less than 2 mg and/or less than 2% w/w of pramipexole

Use the average of the individual results obtained in the test for Uniformity of content.

For tablets containing the equivalent of 2 mg or more and 2% w/w of pramipexole

Weigh and powder 20 tablets. Carry out the method for [liquid chromatography, Appendix III D](#), using the following solutions in solution A, as described under Related substances.

- (1) Shake a quantity of powdered tablets containing the equivalent of 0.26 mg of pramipexole with 100 mL solution A with the aid of ultrasound. Extract 10 mL, filter and dilute the filtrate, if necessary, to produce a solution containing the equivalent of 0.00013% w/v of pramipexole.
- (2) 0.00013% w/v of [pramipexole BPCRS](#).
- (3) 0.0003% w/v of [pramipexole BPCRS](#) and 0.0003% w/v of [pramipexole impurity A BPCRS](#).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Uniformity of content may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the [resolution](#) between the peaks due to impurity A and pramipexole is at least 6.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{10}H_{17}N_3S$ in the tablets using the declared content of $C_{10}H_{17}N_3S$ in [pramipexole BPCRS](#).

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B and C listed under Pramipexole Dihydrochloride Monohydrate.