Pivmecillinam Tablets

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

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<th>EAG/Panel/Working Party</th>
<th>Antibiotics</th>
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<td>Deadline for Comment</td>
<td>31st December 2021</td>
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<td>Target Publication Date (subject to change)</td>
<td>BP 2023</td>
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<td>Notes</td>
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If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

Action and use

Penicillin Antibacterial.

DEFINITION

Pivmecillinam Tablets contain Pivmecillinam Hydrochloride.

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

Content of pivmecillin hydrochloride, C₂₁H₃₄ClIN₅O₅S, HCl

93.5 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.2 g of Pivmecillinam Hydrochloride with 20 mL of dichloromethane, filter and evaporate the filtrate to dryness. The infrared absorption spectrum, Appendix II A, is concordant with the reference spectrum of pivmecillin hydrochloride (RS XXX). In the preparation of the disc, avoid excessive grinding when triturating the substance being examined with potassium chloride.

TESTS

Dissolution
Comply with the dissolution test for tablets and capsules, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of 0.1M hydrochloric acid, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in solution A. Prepare the solutions immediately before use and protected from light.

Solution A: 45 volumes of acetonitrile and 55 volumes of a 1.35% w/v solution of potassium dihydrogen orthophosphate previously adjusted to pH 3.0 with orthophosphoric acid.

(1) After 15 minutes withdraw a sample of the medium and filter. Dilute with the dissolution medium if necessary, to produce a solution expected to contain 0.01% w/v of Pivmecillinam Hydrochloride.
(2) 0.01% w/v of pivmecillinam hydrochloride BPCRS.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.0 mm) packed with octadecylsilica gel for chromatography (5 µm) (Kromasil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Dissolve 0.55 g of tetraethylammonium hydrogen sulfate and 1.0 g of tetramethylammonium hydrogen sulfate in solution A, and dilute to 1000 mL with solution A.

DETERMINATION OF CONTENT

Calculate the total content of C_{21}H_{34}ClN_{3}O_{5}S.HCl in the medium from the chromatograms obtained and using the declared content of C_{21}H_{34}ClN_{3}O_{5}S, HCl in pivmecillinam hydrochloride BPCRS.

LIMITS

The amount of pivmecillinam hydrochloride released is not less than 80% (Q) of the stated amount.

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in solution A. Prepare the solutions immediately before use and protected from light.

(1) Disperse with the aid of ultrasound a quantity of the powdered tablets containing 0.1 g of Pivmecillinam Hydrochloride with 100 mL. Mix and filter through a 0.45-µm filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes.

(3) 0.01% w/v each of *pivmecillinam hydrochloride BPCRS* and *pivmecillinam impurity C EPCRS*.

(4) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used, allowing the chromatography to proceed for three times the retention time of pivmecillinam.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to pivmecillinam (retention time about 5 minutes) are: impurity C, about 1.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between pivmecillinam and impurity C is at least 3.5.

LIMITS

In the chromatogram obtained with solution (1):

- the area of any *secondary peak* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);
- the sum of the areas of any *secondary peaks* is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (3%).

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

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography, Appendix III D*, using the following solutions in solution A. Prepare the solutions immediately before use and protected from light.

(1) Disperse with the aid of ultrasound a quantity of the powdered tablets equivalent to 0.5 g of Pivmecillinam Hydrochloride with sufficient solvent to produce 250 mL. Filter through a 0.45-µm filter (Whatman GF/C is suitable) and dilute 1 volume of the filtrate to 20 volumes.

(2) 0.01% w/v of *pivmecillinam hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{34}ClIN_3O_5S$, HCl in the tablets from the chromatograms obtained and using the declared content of $C_{21}H_{34}ClIN_3O_5S$, HCl in *pivmecillinam hydrochloride BPCRS*.

IMPURITIES
The impurities limited by the requirements of this monograph include those listed under Pivmecillinam Hydrochloride.