Pivmecillinam Tablets

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

<table>
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<th>EAG ABS</th>
<th>Antibiotics</th>
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<td>Deadline for Comment</td>
<td>31st December 2020</td>
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<td>Notes:</td>
<td>New monograph</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 complies with the requirements stated under Tablets and with the following requirements.

Content of pivmecillinam hydrochloride, $\text{C}_{21}\text{H}_{34}\text{ClN}_{3}\text{O}_{5}\text{S}$

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 pivmecillinam 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.
(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 prepared in the mobile phase. Prepare the solutions immediately before use and protected from light.

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

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column 15 cm × 4.6 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 2.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for three times the retention time of pivmecillinam.

MOBILE PHASE

45 volumes of a solution containing 0.02M potassium dihydrogen phosphate and 0.005M sodium octanesulfonate previously adjusted to pH 3.0 with dilute phosphoric acid, and 55 volumes of acetonitrile

SYSTEM SUITABILITY

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

DETERMINATION OF CONTENT

Calculate the total content of pivmecillinam hydrochloride, C_{21}H_{34}ClN_{3}O_{5}S, in the medium from the chromatograms obtained and using the declared content of C_{21}H_{34}ClN_{3}O_{5}S, 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 prepared in a mixture of 40 volumes of acetonitrile and 60 volumes of water. 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 with the following modification:

**MOBILE PHASE**

35 volumes of a solution containing 0.02M potassium dihydrogen phosphate and 0.005M sodium octanesulfonate previously adjusted to pH 3.0 with dilute phosphoric acid, and 65 volumes of acetonitrile

**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 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%).

**Water**

Not more than 3.5% w/w, Appendix IX C. Use 0.2 g.

**ASSAY**

Weigh and powder 20 tablets. Carry out the method for liquid chromatography, Appendix III D, using the following solutions prepared in a mixture of 40 volumes of water and 60 volumes of acetonitrile. Prepare the solutions immediately before use and protected from light.

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

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

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

**CHROMATOGRAPHIC CONDITIONS**

The chromatographic conditions described under Dissolution may be used.

**DETERMINATION OF CONTENT**

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

**IMPURITIES**

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