Status: Effectivity information can only be shown for content published to the website.

Update information can only be shown for content published to the website.

Pivmecillinam Tablets

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

EAG ABS	Antibiotics
Contact Details	stephen.maddocks@mhra.gov.uk hannah.bowden@mhra.gov.uk
Deadline for Comment	31st December 2020
Target Publication (subject to change)	BP 2022
Notes:	New monograph 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, $C_{21}H_{34}ClN_3O_5S$

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.

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 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 *octadecylsilyl silica 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, $C_{21}H_{34}ClN_3O_5S$, in the medium from the chromatograms obtained and using the declared content of $C_{21}H_{34}ClN_3O_5S$, 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 in *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, $C_{21}H_{34}ClN_3O_5S$, in the tablets from the chromatograms obtained and using the declared content of $C_{21}H_{34}ClN_3O_5S$, in *pivmecillinam hydrochloride BPCRS*.

IMPURITIES

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