DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Analytical profile of Ivabradine Tablets

Analytical Profile No: Ivab 077/078/AP 086

Ivabradine Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Ivabradine.

Usual Strength: Ivabradine 5mg, 7.5mg

1. Identification:

In the Assay, the principle peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests:

2. Dissolution: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900ml of 0.05M Phosphate buffer pH 6.8 prepared by dissolving 6.8 g of Potassium Dihydrogen Orthophosphate and 0.896g of Sodium Hydroxide pellet in 1000ml water and adjusting pH to 6.8 with 0.2M NaOH or 0.1M HCl.

Speed and Time: 50 rpm and 30 minutes

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography.

2.2 Test Solution: Dilute the filtrate, if necessary, with dissolution medium.

2.3 Reference Solution: Weigh accurately about 27.5 mg of Ivabradine HCl WS in 100 ml volumetric flask. Dissolve in 70ml of dissolution medium and make up the volume to 100 ml with dissolution medium. Further dilute 2 ml of the solution to 100 ml with dissolution medium.

2.4 Procedure: Use the chromatographic system as described in the Assay.

Inject the reference solution and the test solution.

2.5 Limit: Not less than 75 percent (D) of the stated amount of Ivabradine.

3. Uniformity of Content

Determine by liquid chromatography, as described in the Assay, using the following solution as the test solution.

Test Solution: Place a tablet in a 100ml volumetric flask, add 70ml of mobile phase, sonicate for 30 minutes to disperse whole tablet. Cool, make up the volume to 100 ml with same solvent and centrifuge.

4. Assay: *Determine by liquid chromatography*

4.1 Test Solution: Transfer 10 intact tablets to a 100ml volumetric flask. Add about 70 ml of mobile phase and sonicate for about 30 mins to dissolve, cool to room temperature and make up the volume to 100 ml with same solvent. Centrifuge and dilute 5 ml of supernatant solution to 50 ml with mobile phase.

4.2 Reference Solution: Weigh accurately about 50 mg of Ivabradine HCl WS in 100ml volumetric flask and dissolve in 70 ml of mobile phase. Make up the volume to 100 ml with same solvent and dilute 5ml of the resulting solution to 50ml with same solvent.

4.3 Chromatographic system:

- **Column:** C18, 25 cm x 4.6 mm, 5µm particle size
- **Flow rate:** 1.2 ml/min
- **Wavelength:** 286 nm
- **Injection volume:** 20 µl
- **Detector:** UV/PDA
- **Column temperature:** 35 °C
- **Mobile Phase:** A mixture of 65 volumes of buffer solution pH 7.0 and 35 volumes of Acetonitrile
- **Buffer solution pH 7.0:** Mix 5 ml of Formic acid to 1000 ml water and adjust pH 7.0 with Ammonia solution

4.4 Procedure: Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0%.

Calculate the content of Ivabradine in the tablet.

5. Other tests: As per pharmacopoeial requirement.