Ticagrelor Tablets

Ticagrelor Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of ticagrelor, C₂₃H₂₈F₂N₆O₄S.

Usual strength. 90 mg.

Identification

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

Tests

Dissolution (2.5.2).

Apparatus No. 1,

Medium. 900 ml of 0.2 per cent v/v of polysorbate 80 in water,

Speed and time. 75 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with dissolution medium if necessary, at the maximum at about 300 nm (2.4.7). Calculate the content of C₂₃H₂₈F₂N₆O₄S in the medium from the absorbance obtained from a solution of known concentration of ticagrelor RS in the same medium.

D. Not less than 75 per cent of the stated amount of C₂₃H₂₈F₂N₆O₄S.

Related substances. Determine by liquid chromatography (2.4.14) as described under Assay with the following modifications.

NOTE — Protect the solutions from light.

Reference solution (a). A solution containing 0.05 per cent w/v of ticagrelor RS and 0.0001 per cent w/v of ticagrelor related compound B RS in the solvent mixture.

Reference solution (b). A 0.0001 per cent w/v solution of ticagrelor RS in the solvent mixture.

Reference solution (c). Dilute 5.0 ml of reference solution (b) to 10.0 ml with the solvent mixture.

Chromatographic system

– mobile phase: A. 1 volume of the buffer solution, 89 volumes of water and 10 volumes of acetonitrile,

– B. 1 volume of the buffer solution, 29 volumes of water and 70 volumes of acetonitrile,

– a gradient programme using the conditions given below,

– flow rate: 1 ml per minute.

<table>
<thead>
<tr>
<th>Time (in min.)</th>
<th>Mobile phase A (per cent v/v)</th>
<th>Mobile phase B (per cent v/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
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<tr>
<td>15</td>
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<td>23</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>28</td>
<td>90</td>
<td>10</td>
</tr>
</tbody>
</table>

Name relative retention time

Ticagrelor 1.0
Ticagrelor related compound B 1.07

¹[(5S,6S,10R,15S)-3-((3-[1R,2S]-2-(3,4-Difluorophenyl)cyclopropyl)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yl)amino]-5-(2-hydroxyethoxy) cyclopentane-1,2-diol.

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to ticagrelor and ticagrelor related compound B is not less than 1.5 in the chromatogram obtained with reference solution (a), the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (b) and the signal to noise ratio for the principal peak is not less than 10 in the chromatogram obtained with reference solution (c).
Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent).

**Other tests.** Comply with the tests stated under Tablets.

**Assay.** Determine by liquid chromatography (2.4.14).

**Solvent mixture.** 35 volumes of acetonitrile and 65 volumes of water.

**Buffer solution.** 1M sodium phosphate, adjusted to pH 3.0 with orthophosphoric acid.

**Test solution.** Weigh and powder 20 tablets. Disperse a quantity of the powder containing 50 mg of Ticagrelor with 60 ml of the solvent mixture, with the aid of ultrasound with intermittent shaking and dilute to 100.0 ml with the solvent mixture.

**Reference solution.** A 0.05 per cent w/v solution of ticagrelor RS in the solvent mixture.

**Chromatographic system**
- a stainless steel column 15 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (1.8 µm),
- column temperature: 55°,
- mobile phase: a mixture of 52 volumes of acetonitrile, 47 volumes of water and 1 volume of the buffer solution,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 242 nm,
- injection volume: 5 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of C₂₃H₂₈F₂N₆O₄S in the tablets.

**Storage.** Store protected from light and moisture, at a temperature not exceeding 30°.