Tofacitinib Tablets

Tofacitinib Citrate Tablets

Tofacitinib Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of tofacitinib, $C_{16}H_{20}N_6O$.

Usual strength. 5 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 (Basket),
Medium. 900 ml of *0.1 M hydrochloric acid,*
Speed and time. 100 rpm and 15 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14)

Test solution. Dilute the filtrate, if necessary with the dissolution medium.

Reference solution. Dissolve a quantity of *tofacitinib citrate IPRS* in the dissolution medium to obtain a solution of concentration similar to the expected concentration of the test solution.

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 75 volumes of a buffer solution prepared by dissolving 1.36 g of *potassium dihydrogen orthophosphate* and 1.75 g of *dipotassium hydrogen orthophosphate* in 1000 ml of *water*, and 25 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, 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 $C_{16}H_{20}N_6O$ in the medium.

Q. Not less than 80 per cent of the stated amount of $C_{16}H_{20}N_6O$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 80 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 6.0 with *potassium hydroxide solution* and 20 volumes of *acetonitrile*.

Test solution. Disperse a quantity of powdered tablets containing 30 mg of Tofacitinib in the solvent mixture, with the aid of magnetic stirrer for about 30 minutes and dilute to 100.0 ml with the solvent mixture, filter.

Reference solution (a). A solution containing 0.0001 per cent w/v, each of, *DCT IPRS* and *diastereomer of tofacitinib citrate impurity IPRS* and 0.05 per cent w/v of *tofacitinib citrate IPRS* in the solvent mixture.

Reference solution (b). Dissolve a suitable quantity of *tofacitinib citrate IPRS* in the solvent mixture to obtain a solution containing 0.0003 per cent w/v of tofacitinib.

Reference solution (c). Dilute 1.0 ml of reference solution (b) to 20.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm), (Such as ACE 5 C-18-PFP),
- column temperature: 35º,
- mobile phase: A. a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*,

B. *acetonitrile*,

– flow rate: 1 ml per minute,
– spectrophotometer set at 210 nm,
– injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	79	21
15	79	21
25	35	65
30	35	65
32	79	21
40	79	21

Name	Relative retention time
Citric acid	0.22
DCT[1]	0.33
Tofacitinib (Retention time: about 11 minutes)	1.0
Diastereomer of tofacitinib citrate[2]*	1.19

*Process impurity include for identification only and not included in the calculation of total degradation products.
[1]N-methyl-N[(3R,4R)-4-methylpiperidin-3yl]-7H-pyrrolo[2,3-d]pyrimidin-4-amine
[2]3-[(3RS, 4SR)-4-Methyl-3- [methyl (7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]piperidin-1-yl]-3- oxopropanenitrile.2-Hydroxy propane-1,2,3-tricarboxylic acid

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to tofacitinib and diastereomer of tofacitinib citrate impurity is not less than 3.5 in the chromatogram obtained with reference solution (a), the column efficiency is not less than 9000 theoretical plates, the tailing factor is not more than 1.5, the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (b) and the signal-to-noise ratio 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 peak corresponding to DCT is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent), the area of any other secondary peak is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent) and the sum of areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (2.0 per cent). Ignore the peak due to citric acid and any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Uniformity of content. Complies with the test stated under Tablets.

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

Test solution. Disperse one intact tablet in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Inject the reference solution and test solution.

Calculate the content of $C_{16}H_{20}N_6O$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Water (2.3.43). Not more than 7.0 per cent, determined on 0.5 g.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of *water* and *acetonitrile.*

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powder containing 50 mg of Tofacitinib in the solvent mixture, with the aid of magnetic stirrer for about 45 minutes and dilute to 200.0 ml with the solvent mixture, filter. Dilute 2.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution. Dissolve a suitable quantity of *tofacitinib citrate IPRS* in the solvent mixture to obtain a solution containing 0.005 per cent w/v of tofacitinib.

Chromatographic system
– a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
– mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 1.36 g of *potassium dihydrogen phosphate* and 1.75 g of *dipotassium hydrogen phosphate* in 1000 ml of *water*, and 20 volumes of *acetonitrile*,

– flow rate: 1.5 ml per minute,
– spectrophotometer set at 215 nm,
– injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, 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 $C_{16}H_{20}N_6O$ in the tablets.

Each mg of tofacitinib citrate, $C_{22}H_{28}N_6O_8$ is equivalent to 0.619 mg of tofacitinib, $C_{16}H_{20}N_6O$.

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

Labelling. The label states the strength in terms of the equivalent amount of Tofacitinib.