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, $C_{22}H_{28}N_6O_8$

Usual strengths. 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. 2,
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 RS* 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 phosphate* and 1.75 g of *dipotassium hydrogen phosphate anhydrous* 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 are 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 $C_{22}H_{28}N_6O_8$ in dissolution medium.
D. Not less than 80 per cent of the stated amounts of $C_{22}H_{28}N_6O_8$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. A mixture of 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 10.0 per cent *potassium hydroxide* solution and 20 volumes of *acetonitrile.*

Test solution. Disperse a quantity of powder containing 31.0 mg of Tofacitinib in the solvent mixture with the aid of magnetic stirrer about 30 minutes and diluted to 100.0 ml with the solvent mixture, filter through 0.45 µm PTFE filter.

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

Reference solution (b). 0.005 per cent w/v of *tofacitinib citrate RS* in the solvent mixture.

Reference solution (c). Dilute 5.0 ml of reference solution (b) to 100.0 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 a ACE 5 C-18-PEP),
- 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
DCT[1]	0.33
N- Acetyl DCT[2]	0.83
Tofacitinib (Retention time: about 11 minutes)	1.0
Diastereomer of Tofacitinib Citrate[3]	1.19

[1]N-methyl-N[(3R,4R)-4-methylpiperidin-3yl]-7H-pyrrolo[2,3-d]pyrimidin-4-amine

Inject the reference solution (a) and (c). The test is not valid unless the resolution between N- Acetyl DCT peak and tofacitinib peak is not less than 3.0, the resolution between tofacitinib peak and diastereomer of tofacitinib citrate impurity is not less than 3.5, the signal to noise ratio is not less than 10 for the tofacitinib peak in the chromatogram obtained with the reference solution (c), the column efficiency is not less than 9000 theoretical plates, the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 5.0 per cent for tofacitinib peak.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of the peaks corresponding to DCT, N- Acetyl DCT and diastereomer of tofacitinib impurity, each of, is not more the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (b) (1.0 per cent) and the sum of areas of all the secondary peaks is not more than 3 times the area of the principal peak in the chromatogram obtained with the reference solution (b) (3.0 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. A mixture of 50 volumes of *water* and 50 volumes of *acetonitrile.*

Test solution. Weigh and transfer 10 intact tablets in the solvent mixture with the aid of magnetic stirrer about 45 minutes and diluted to 200.0 ml with the solvent mixture. Filter and dilute 10.0 ml of this solution to 50.0 ml with the solvent mixture.
Reference solution. A 0.005 per cent w/v solution of *Tofacitinib citrate RS* in the solvent mixture.

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 anhydrous* 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 $C_{22}H_{28}N_6O_8$ in the tablets.

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