British Pharmacopoeia | **Quality standards**

Edition: BP 2025 (Ph. Eur. 11.6 update)

Teriflunomide Tablets

[General Notices](#)

(Ph. Eur. monograph 3037)

Action and use

Immunomodulator; treatment of multiple sclerosis.

Ph Eur

DEFINITION

Tablets containing *[Teriflunomide (3036)](#)*, for human use.

They comply with the monograph [Tablets (0478)](#) and the following additional requirements.

Content

95.0 per cent to 105.0 per cent of the content of teriflunomide ($C_{12}H_9F_3N_2O_2$) stated on the label.

IDENTIFICATION

A.   Record the UV spectrum of the principal peak in the chromatograms obtained with the solutions used in the assay, with a diode array detector, in the range of 200-400 nm.

Results   The UV spectrum of the principal peak in the chromatogram obtained with the test solution is similar to the UV spectrum of the principal peak in the chromatogram obtained with reference solution (d).

B.   Examine the chromatograms obtained in the assay.

Results   The principal peak in the chromatogram obtained with the test solution is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (d).

TESTS

Related substances

Liquid chromatography (*[2.2.29](#)*).

Buffer solution   3.85 g/L solution of *[ammonium acetate R](#)* adjusted to pH 5.5 with *[glacial acetic acid R](#)*.

Solvent mixture   Buffer solution, *[acetonitrile R](#)* (20:80 *V/V*).

Test solution   To 10 tablets, add a volume of the solvent mixture equivalent to about half of the final volume. Dissolve the tablets by shaking for approximately 20 min and sonicating for about 3 min. Dilute to volume with the solvent mixture to obtain a concentration of teriflunomide of 0.7 mg/mL and filter. Dilute 3.0 mL of the filtrate to 10.0 mL with the solvent mixture.

Reference solution (a)   Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture.

Reference solution (b)   Dissolve 10 mg of <u>leflunomide impurity A CRS</u> (teriflunomide impurity A) in <u>acetonitrile R</u> and dilute to 250 mL with the same solvent. Dilute 1 mL of the solution to 200 mL with the solvent mixture.

Reference solution (c)   Dissolve 5 mg of <u>teriflunomide impurity B CRS</u> in <u>acetonitrile R</u> and dilute to 100 mL with the same solvent. Dilute 2 mL of the solution to 50 mL with the solvent mixture. To 1 mL of this solution add 1 mL of reference solution (b) and dilute to 10 mL with the solvent mixture.

Reference solution (d)   Dissolve 21.0 mg of <u>teriflunomide for assay CRS</u> in 40 mL of the solvent mixture and dilute to 100.0 mL with the solvent mixture.

Reference solution (e)   Dilute 1.0 mL of reference solution (a) to 10.0 mL with the solvent mixture.

Column:

    — *size*: *l* = 0.15 m, Ø = 4.6 mm;

    — *stationary phase*: <u>end-capped solid core octadecylsilyl silica gel for chromatography R</u> (2.7 μm);

    — *temperature*: 40 °C.

Mobile phase:

    — *mobile phase A*: <u>acetonitrile for chromatography R</u>, buffer solution (10:90 *V/V*);

    — *mobile phase B*: buffer solution, <u>acetonitrile for chromatography R</u> (10:90 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	76	24
2 - 12	76 → 23	24 → 77

Flow rate   1.0 mL/min.

Detection   Spectrophotometer at 249 nm.

Injection   5 μL of the test solution and reference solutions (c) and (e).

Identification of impurities   Use the chromatogram obtained with reference solution (c) to identify the peaks due to impurities A and B.

Relative retention   With reference to teriflunomide (retention time = about 5 min): impurity B = about 1.5; impurity A = about 1.6.

System suitability   Reference solution (c):

    — <u>resolution</u>: minimum 1.5 between the peaks due to impurities B and A;

    — <u>signal-to-noise ratio</u>: minimum 10 for the peak due to impurity A.

Calculation of percentage contents:

    — for each impurity, use the concentration of teriflunomide in reference solution (e).

Limits:

    — *impurity A*: maximum 0.01 per cent;

    — *impurity B*: maximum 0.30 per cent;

    — *unspecified impurities*: for each impurity, maximum 0.10 per cent;

    — *total*: maximum 0.40 per cent;

    — *reporting threshold*: 0.05 per cent; do not disregard the peak due to impurity A.

Dissolution[1] (<u>2.9.3, Apparatus 2</u>).

Dissolution medium 6.8 g/L solution of *potassium dihydrogen phosphate R* adjusted to pH 6.8 with a 200 g/L solution of *sodium hydroxide R*. Use 1000 mL of the medium.

Rotation speed 50 r/min.

Time 30 min.

Analysis Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

Test solution Samples withdrawn from the dissolution vessel and filtered.

Measure the absorbance of the solutions at the absorption maximum at 292 nm.

Calculate the amount of dissolved teriflunomide ($C_{12}H_9F_3N_2O_2$), expressed as a percentage of the content stated on the label, taking the specific absorbance to be 854.

Acceptance criterion:

— Q = 75 per cent after 30 min.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Injection Test solution and reference solution (d).

System suitability Reference solution (d):

— *symmetry factor*: maximum 2.0 for the peak due to teriflunomide;

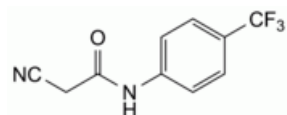— *repeatability*: maximum relative standard deviation of 1.5 per cent determined on 6 injections.

Calculate the percentage content of teriflunomide ($C_{12}H_9F_3N_2O_2$) taking into account the assigned content of *teriflunomide for assay CRS*.

IMPURITIES

Specified impurities A, B.
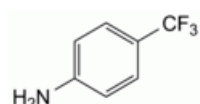
A. 4-(trifluoromethyl)aniline (leflunomide impurity A),

B. 2-cyano-*N*-[4-(trifluoromethyl)phenyl]acetamide.

Ph Eur

[1] The test approved in the marketing authorisation is to be used for routine quality control to confirm batch-to-batch consistency. For more information please consult Ph. Eur. *1. General Notices.*

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