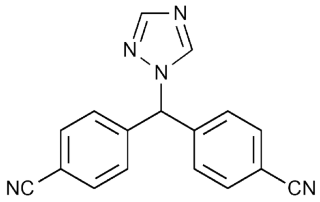
Letrozole Tablets (USP)



Letrozole is an oral non-steroidal aromatase inhibitor for the treatment of hormonally-responsive breast cancer after surgery.

Estrogens are produced by the conversion of androgens through the activity of the aromatase enzyme. Estrogens then bind to an estrogen receptor, which causes cells to divide.

Letrozole prevents the aromatase from producing estrogens by competitive, reversible binding to the heme of its cytochrome P450 unit. The action is specific, and Letrozole does not reduce production of mineralo- or corticosteroids.

Original Manufacturer:	Novartis (patent expired 2011)
Brand Name:	Femara

Drug dissolution testing has been carried out following the experimental conditions in the USP37-NF32 monograph for Letrozole Tablets (*using an isocratic HPLC method with RP-18 endcapped columns and thus scalable*).

We have transferred this method to a monolithic column. The new method is fast, having improved chromatographic efficiency, lower column backpressure, and still meeting all method performance criteria compared to the prescribed column.

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Dissolution <711>

HPLC

Test 1
Medium: 0.1 N hydrochloric acid; 500 mL
Apparatus 2: 100 rpm
Time: 30 min
Standard solution: Transfer USP Letrozole RS to a suitable volumetric flask, dissolve in acetonitrile equivalent to 10% of the final volume, and dilute with Medium to volume to obtain a solution of 0.05 mg/mL of letrozole. Dilute this solution with Medium to obtain a solution of 0.005 mg/mL of letrozole.
Sample solution: Centrifuge a portion of the solution under test at 4000 rpm for 5 min.
Mobile phase and Chromatographic system: Proceed as directed in the Assay, except use an injection volume of 200 µL.

Assay
Mobile phase: Acetonitrile and water (48:52)
Diluent: Acetonitrile and water (30:70)
Standard stock solution: 0.2 mg/mL of USP Letrozole RS in Diluent.
[Note—Dissolve letrozole in acetonitrile, and then dilute with water.]
Standard solution: 10 µg/mL of USP Letrozole RS in Mobile phase, from the Standard stock solution
Sample stock solution: Equivalent to 50 mg of letrozole from Tablets, in a 250-mL volumetric flask. Add 20 mL of water, and shake for 5 min to dissolve the Tablets. Add 75 mL of acetonitrile, shake for 30 min, and dilute with water to volume. Centrifuge a portion of the solution.
Sample solution: 10 µg/mL of letrozole in Mobile phase, from the Sample stock solution

Chromatographic system (See Chromatography 621 , System Suitability.)
Detector: UV 230 nm
Column: 125x4.6 mm; 5 µm packing L1
Flow rate: 1 mL/min
Injection volume: 20 µL
System suitability (Sample: Standard solution)

Suitability requirements
Tailing factor: 0.8-1.5
Relative standard deviation: NMT 2.0%

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of letrozole ($C_{17}H_{11}N_5$) dissolved:

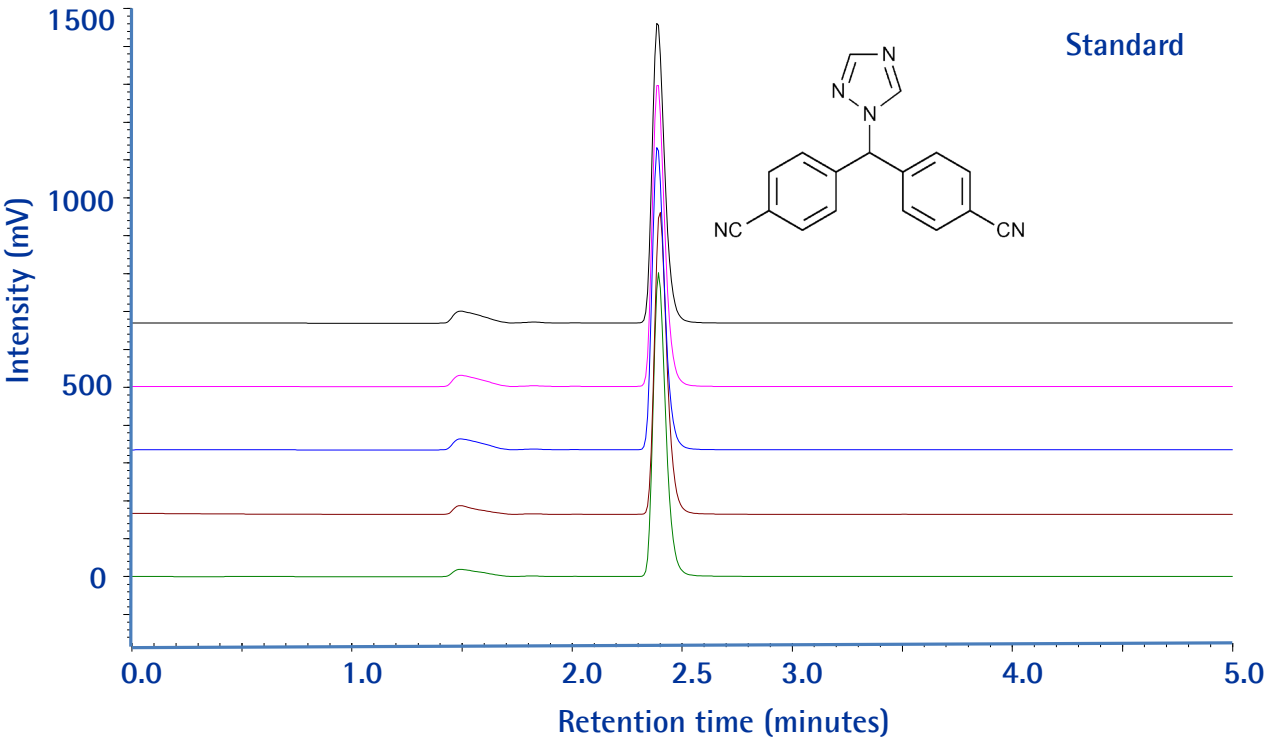
$$\text{Result} = (rU/rS) \times (CS/L) \times V \times 100$$

rU = peak response from the Sample solution
rS = peak response from the Standard solution
CS = concentration of USP Letrozole RS in the Standard solution (mg/mL)
L = label claim (mg/Tablet)
V = volume of Medium, 900 mL
Tolerances: NLT 80% (Q) of the labeled amount of letrozole ($C_{17}H_{11}N_5$) is dissolved.

Letrozole Tablets (USP)

Chromolith® HighResolution RP-18 endcapped

Column:	Chromolith® HighResolution RP-18e, 100x4.6 mm	1.52022.0001
Injection:	10 µl	
Detection:	Shimadzu 2010CHT, UV 230 nm	
Cell:	10 µL	
Flow Rate:	1 mL/min	
Mobile Phase:	Acetonitrile and water 48:52 (v/v)	
Temperature:	25 °C	
Diluent:	0.1 N HCl 500 ml , 100 rpm for 30 minutes	
Sample soltion:	Filter the solution through 0.45 µm Millex HV Filter (PVDF Filter)	
Pressure Drop:	92 Bar (1334psi)	



Suitability requirements
Tailing factor: 0.8-1.5

Chromatographic Data :

No.	Compound	Retention Time (min)	Tailing factor	Theoretical Plate
1	Letrozole	2.38	1.4	6500

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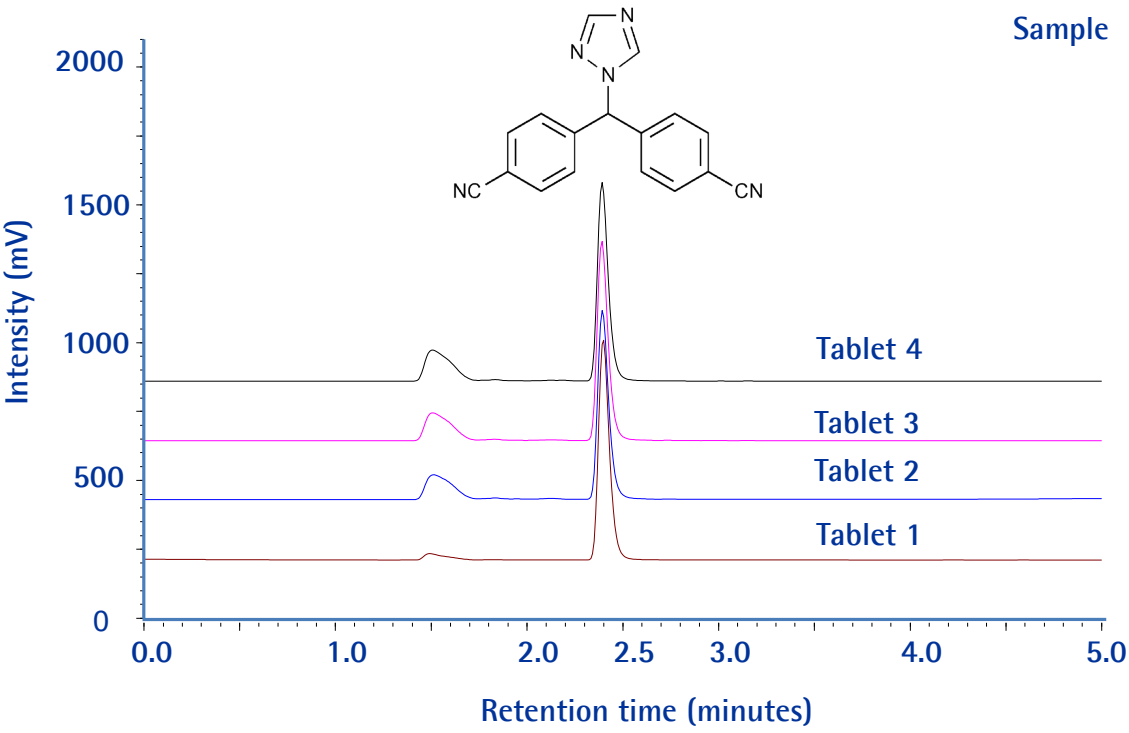
Chromolith® HighResolution RP-18 endcapped



Result = (rU/rS) × (CS/L) ×V× 100

RU	RS	CS	V	L	Dissolution (%)
3151347	2901103	0.005	500	40	92
3183314	2884977	0.005	500	40	91.4
3164150	2911107	0.005	500	40	92.2
3202526	2784812	0.005	500	40	88.2
3205292	2911400	0.005	500	40	92.2
Average					91.2±1.7

Tolerances: NLT 80% (Q) of the labeled amount of Letrozole (C17H11N5) is dissolved.

* Label claim of the Letrozole Tablet = 2.5 mg