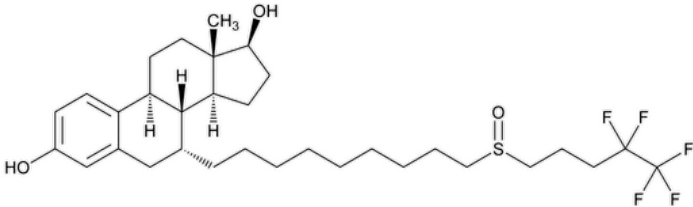


Status: Currently Official on 14-Feb-2025  
Official Date: Official as of 01-Feb-2022  
Document Type: USP Monographs  
DocId: GUID-AEF1B8C2-0ED5-4A68-A843-739B9AEB5AEC\_3\_en-US  
DOI: [https://doi.org/10.31003/USPNF\\_M2002\\_03\\_01](https://doi.org/10.31003/USPNF_M2002_03_01)  
DOI Ref: h3url

© 2025 USPC  
Do not distribute

# Fulvestrant

Change to read:



$C_{32}H_{47}F_5O_3S$  ▲606.78▲ (ERR 1-Feb-2022)  
Estra-1,3,5(10)-triene-3,17-diol, 7-[9-[(4,4,5,5,5-pentafluoropentyl)sulfinyl]nonyl]-, (7α,17β)-;  
7α-[9-[(4,4,5,5,5-Pentafluoropentyl)sulfinyl]non yl]estra-1,3,5(10)-triene-3,17β-diol CAS RN®: 129453-61-8; UNII: 22X328QOC4.  
» Fulvestrant is a mixture of the diastereoisomers A and B. It contains not less than 97.0 percent and not more than 102.0 percent of  $C_{32}H_{47}F_5O_3S$ , calculated on the anhydrous basis.

**Packaging and storage**—Preserve in well-closed, light-resistant containers. Store refrigerated at 2° to 8°.

**USP REFERENCE STANDARDS (11)**—

USP Fulvestrant RS  
USP Fulvestrant System Suitability Mixture RS

Contains fulvestrant isomer A, fulvestrant isomer B, and fulvestrant β-isomer.

**Identification**—

**A:** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197K](#)—

Spectral range: 4000 to 400 cm<sup>-1</sup>.

**B:** The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation, as obtained in the Assay.

**SPECIFIC ROTATION (781S):** between +108° and +115° measured at 365 nm.

Test solution: 20 mg per mL, in methanol.

**WATER DETERMINATION, Method Ic (921):** not more than 0.5%.

**RESIDUE ON IGNITION (281):** not more than 0.1%.

Change to read:

**Related compounds**—

Mobile phase and System suitability solution—Prepare as directed in the Assay.

Standard solution—Prepare as directed for the Standard preparation in the Assay.

Test solution—Use the Assay preparation.

Chromatographic system (see [CHROMATOGRAPHY \(621\)](#))—Proceed as directed in the Assay.

Procedure—Separately inject equal volumes (about 10 μL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of each impurity in the portion of Fulvestrant taken by the formula:

$$100(CV/W)(1/F)(r_i/r_s)$$

in which C is the concentration, in mg per mL, of [USP Fulvestrant RS](#) in the Standard solution; V is the volume, in mL, of the Test solution; W is the weight, in mg, of Fulvestrant taken to prepare the Test solution; F is the relative response factor as listed in the accompanying table;  $r_i$  is the individual peak response for each impurity obtained from the Test solution; and  $r_s$  is the fulvestrant peak response obtained from the Standard solution. Disregard impurity peaks less than 0.05%. The limits are as shown in the accompanying table.

| Compound                        | Relative Retention Time | Relative Response Factor | Limit (%) |
|---------------------------------|-------------------------|--------------------------|-----------|
| 6-Keto-fulvestrant <sup>1</sup> | 0.5                     | 2.9                      | 0.1       |

| Compound                              | Relative Retention Time | Relative Response Factor | Limit (%) |
|---------------------------------------|-------------------------|--------------------------|-----------|
| Δ6,7-Fulvestrant <sup>2</sup>         | 0.9                     | 3.3                      | 0.1       |
| Fulvestrant                           | 1.0                     | 1.0                      | —         |
| Fulvestrant sulfone <sup>3</sup>      | 1.2                     | 1.0                      | 0.2       |
| Fulvestrant extended <sup>4</sup>     | 1.7                     | 1.0                      | 0.3       |
| Fulvestrant sterol dimer <sup>5</sup> | 1.9                     | 1.0                      | 0.8       |
| Fulvestrant β-isomer <sup>6</sup>     | 1.1                     | —                        | *         |
| Any individual unspecified impurity   | —                       | 1.0                      | 0.1       |
| Total impurities                      | —                       | —                        | 1.0       |

\* Fulvestrant β-isomer, a component of [USP Fulvestrant System Suitability Mixture RS](#), is not a specified impurity.

▲<sup>1</sup> 7α-{9-[(4,4,5,5,5-Pentafluoropentyl)sulfinyl]nonyl}estra-1,3,5(10)-triene-6-one-3,17β-diol▲ (ERR 1-Feb-2022)

▲<sup>2</sup> 7-[(4,4,5,5,5-Pentafluoropentyl)sulfinyl]nonyl}estra-1,3,5(10),6-tetraene-3,17β-diol▲ (ERR 1-Feb-2022)

▲<sup>3</sup> 7α-{9-[(4,4,5,5,5-Pentafluoropentyl)sulfonyl]nonyl}estra-1,3,5(10)-triene-3,17β-diol▲ (ERR 1-Feb-2022)

▲<sup>4</sup> 7α-{9-[9-[(4,4,5,5,5-pentafluoropentyl)sulfinyl]nonylsulfinyl]nonyl}estra-1,3,5(10)-triene-3,17β-diol▲ (ERR 1-Feb-2022)

▲<sup>5</sup> 7α,7α-Nonamethylenebis[estra-1,3,5(10)-triene-3,17β-diol]▲ (ERR 1-Feb-2022)

▲<sup>6</sup> 7β-{9-[(4,4,5,5,5-Pentafluoropentyl)sulfinyl]nonyl}estra-1,3,5(10)-triene-3,17β-diol▲ (ERR 1-Feb-2022)

#### Diastereoisomer ratio—

**Mobile phase**—Prepare a filtered and degassed mixture of 2-methylpentane and dehydrated alcohol (880:120). Make adjustments if necessary (see *System Suitability* under [Chromatography \(621\)](#)).

**System suitability solution**—Dissolve a suitable quantity of [USP Fulvestrant System Suitability Mixture RS](#) in *Mobile phase* to obtain a solution containing 1 mg of [USP Fulvestrant System Suitability Mixture RS](#) per mL.

**Test solution**—Transfer about 20 mg of Fulvestrant, accurately weighed, to a 20-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

**Chromatographic system** (see [CHROMATOGRAPHY \(621\)](#))—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains 10-μm packing L51. The flow rate is about 1 mL per minute. The column temperature is maintained at 40°.

Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure*: the resolution, *R*, between fulvestrant isomer A and fulvestrant isomer B is not less than 1.3; and the tailing factor for fulvestrant isomer B is not more than 1.5.[NOTE—For the purpose of peak identification, the retention times are about 20 minutes for fulvestrant isomer B and 23 minutes for fulvestrant isomer A.]

**Procedure**—Inject a volume (about 10 μL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the responses for the two fulvestrant isomer peaks. Calculate the content of fulvestrant isomer A or fulvestrant isomer B, as a percentage, by the formula:

$$100(r_i/r_s)$$

in which  $r_i$  is the peak response of either fulvestrant isomer A or fulvestrant isomer B; and  $r_s$  is the total peak response of both fulvestrant isomer A and fulvestrant isomer B: between 42% and 48% of fulvestrant isomer A and between 52% and 58% of fulvestrant isomer B is obtained.

#### Assay—

**Solution A**—Prepare a filtered and degassed mixture of water, acetonitrile, and methanol (410:320:270).

**Solution B**—Prepare a filtered and degassed mixture of acetonitrile, methanol, and water (490:410:100).

**Mobile phase**—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under [Chromatography \(621\)](#)).

**System suitability solution**—Dissolve suitable quantities of [USP Fulvestrant System Suitability Mixture RS](#) in methanol to obtain a solution containing about 10 mg of [USP Fulvestrant System Suitability Mixture RS](#) per mL.

**Standard preparation**—Dissolve an accurately weighed quantity of [USP Fulvestrant RS](#) in methanol to obtain a solution having a known concentration of about 10 mg per mL.

**Assay preparation**—Transfer about 100 mg of Fulvestrant, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.