Fulvestrant Injection

Published on: 01.08.2024 **Last date for comments:** 14.09.2024

This draft proposal contains monograph text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
Document version	2.0
Monograph proposed for inclusion	IP 2026
Tentative effective date of monograph	July, 2026
First draft published on IPC website for public comments	06.06.2024
Draft revision published on IPC website for public comments	01.08.2024
Further follow-up action as required.	

Fulvestrant Injection

Fulvestrant Injection is a sterile solution of Fulvestrant in Water for Injections.

Fulvestrant Injection contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of fulvestrant, $C_{32}H_{47}F_5O_3S$.

Usual strength. 50 mg per ml.

Identification

A. Condition a silica solid phase extraction (SPE) cartridge with 10 ml of a mixture of 35 volumes of *ether* and 65 volumes of *methylpentane* (solvent mixture) at a flow rate of about 5 ml per minute. Dilute a volume of the injection containing 10 mg of fulvestrant to 100.0 ml with the solvent mixture. Without delay, as fulvestrant may precipitate out of solution, load 1 ml of the solution onto the SPE cartridge at a flow rate of about 1 ml per minute. Wash first with 10 ml of the solvent mixture at a flow rate of about 5 ml per minute and then with 10 ml of *ether* at a flow rate of about 1 ml per minute to remove most of the excipients. Discard the washings. Elute with 10 ml of *ether* at a flow rate of about 1 ml per minute. The volumes used for washing and elution may be adjusted. Usually, 5 to 15 ml is sufficient to wash the cartridge and 10 to 20 ml is used for the elution. Collect the eluate and evaporate to dryness under a steam of nitrogen. (fulvestrant may precipitate out of the solution). The residue of precipitate complies with the following test.

   Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *fulvestrant IPRS* or with the reference spectrum of fulvestrant.

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Dilute a volume of the injection containing 50 mg of Fulvestrant to 5.0 ml with *methanol.*

Reference solution (a). A 1.0 per cent w/v of *fulvestrant IPRS* in *methanol*.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with *methanol*. Dilute 2.0 ml of the solution to 10.0 ml with *methanol*.

Reference solution (c). Dissolve 10 mg of *fulvestrant for system suitability IPRS (containing impurity A, B, C and D)* in 1 ml of *methanol*.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with end capped octylsilane bonded to porous silica (3.5 µm),
- column temperature: 40°,
- mobile phase: A. a mixture of 41 volumes of *water*, 32 volumes of *acetonitrile* and 27 volumes of *methanol,*
  B. a mixture of 49 volumes of *acetonitrile*, 41 volumes of *methanol* and 10 volumes of *water*,
- a gradient programme using the conditions given below,
- flow rate: 2 ml per minute,
- spectrophotometer set at 225 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile Phase B (per cent v/v)
0	100	0
25	100	0
55	0	100
65	0	100
65.1	100	0

70	100	0

Name	Relative retention time
Fulvestrant (Retention time: about 22 minutes)	1.0
Fulvestrant impurity A[1*]	1.1
Fulvestrant impurity B[2]	1.2
Fulvestrant impurity C[3*]	1.6
Fulvestrant impurity D[4*]	1.8

*Process related impurity included for identification only, not to be calculated and included in total degradation product.
[1]7β-[9-[(RS)-4,4,5,5,5-pentafluoropentane-1-sulfinyl]nonyl]estra-1,3,5(10)-triene-3,17β-diol (7β-fulvestrant),
[2]7α-[9-(4,4,5,5,5-pentafluoropentane-1-sulfonyl)nonyl]estra-1,3,5(10)-triene-3, 17β-diol,
[3]7ξ-[9-[(≡)-9-[(≡)-4,4,5,5,5-pentafluoropentane-1-sulfinyl]nonane-1-sulfinyl]nonyl]estra-1,3,5(10)-triene-3,17β-diol,
[4]7ξ,7′ξ-nonane-1,9-diyldi(estra-1,3,5(10)-triene-3, 17β-diol).

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to fulvestrant and fulvestrant impurity A is not less than 1.5.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to fulvestrant impurity B is not more than 5 times 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 reference solution (b) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.2 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances.

Inject reference solution (a). The test is not valid unless the relative standard deviation for replicate injections is not more than 1.0.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{32}H_{47}F_5O_3S$ in the injection.

Storage. Store protected from light, in a sterile, tamper evident container, at a temperature 2° to 8°.