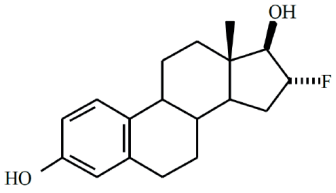
^{18}F fluoroestradiol

^{18}F-FES

[^{18}F]FES (16α-fluoroestradiol) is a lipophilic molecule that acts similarly to estradiol *in vivo* and binds to estrogen receptors. This radiopharmaceutical is under investigation as a noninvasive diagnostic agent for noninvasive assessment of the estrogen receptor content of tumours using positron emission tomography (PET) imaging. The [^{18}F]fluoroestradiol is a sterile, IV injectable aqueous solution with a volume of ≤20 ml containing <10% ethanol (v:v). The injected dose of [^{18}F]FES is generally 200 MBq with an allowable range 100-225 MBq of [^{18}F]fluoroestradiol. The mass of injected drug is ≤5 µg (≤1 nmol) of FES.

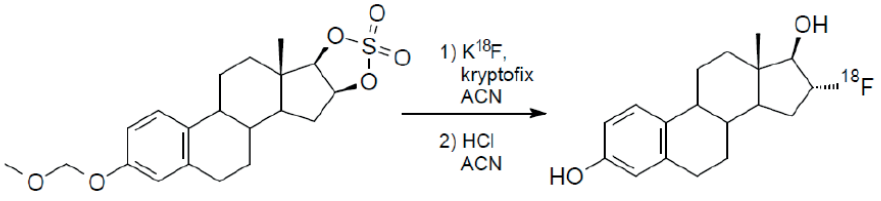


1. Indications

This radiopharmaceutical is under investigation as a noninvasive diagnostic agent for noninvasive assessment of the estrogen receptor content of tumours using positron emission tomography (PET) imaging.

2. Preparation

Briefly, the process of manufacturing [^{18}F]FES consists of the following general steps: Proton bombardment of enriched [O-^{18}]H_2O to produce [^{18}F]]fluoride ion; [^{18}F]fluoride is then allowed to react with 3-O-methoxymethyl-16,17-O-sulfuryl-16-epiestriol, followed by removal of the MOM protecting group and the sulfate group by acid hydrolysis.



3. Quality control

Appearance, pH, radiochemical purity, radiochemical identity, radionuclidic identity, specific activity.

Impurities: Kryptofix, ^{18}F-fluoride, total unknown impurities, acetonitrile, methanol, ethanol, endotoxin.

Post release: sterility, radionuclidic purity.

4. Interactions
Estrogen receptor binding drugs.

5. Adverse reactions
Other than infrequent transient intravenous site discomfort and an "alcohol taste", there have been no adverse events related to [^{18}F]FES administration.

6. Biodistribution & pharmacokinetics
[^{18}F]fluoroestradiol (FES) is a radiopharmaceutical designed for imaging estradiol binding to estrogen receptors (ERs) in vivo. Its molecular weight is 290,4 Daltons. FES has chemical properties very similar to estradiol. The relative binding affinity (RBA, FES/estradiol) for the estrogen receptor is 0,813. The metabolism of FES and estradiol are similar with elimination primarily by conjugation in the liver, followed by renal clearance of the glucuronide. Measurements of the relative binding affinity for the blood transport protein, sex hormone binding globulin (SHBG), was 10% relative to estradiol. An average of 45% of circulating FES is bound to SHBG, similar to estradiol.
Typical blood FES concentration after a 6 mCi injection is 1 µCi/ml (<3 pmol/ml) peak, and by 60 min after injection it is <150 fmol/ml. The metabolism of estradiol has been well characterized. Like other steroids, estradiol has high uptake in the liver. Metabolism occurs largely in the liver, with two key components: (1) oxidation at the 17 position to form the estrone and (2) hydroxylation at the 2 and 16 positions to form hydroxy estradiols or estrones. FES is rapidly metabolized to polar species, with less than 20% of blood radioactivity in the form of [^{18}F]FES by 60 min after injection. There is also net clearance of both FES and labeled metabolites from the blood via hepatic uptake, biliary excretion, and urinary excretion of polar conjugates. By 120 min after injection, circulating FES is less than 5% of peak values, and the total of FES and labeled metabolites is less than 40% of the peak. The liver rapidly takes up FES with subsequent excretion into bile. From sequential images of the biodistribution of FES using PET, it was shown that FES passed into the bile and moved through the small intestine. Very little, if any, radioactivity was seen in the large intestine, suggesting highly efficient enterohepatic circulation, similar to that of estradiol.

7. Stability
Physical half-life of [^{18}F]FES is 110 min. The injection takes place immediately after production. The stability of the product has been investigated and the product is stable for at least 24 h after production in the current formulation. This allows transportation of the product to other qualified hospitals for clinical use in those hospitals within the product's expiry time.