Estradiol Vaginal Inserts

Type of Posting: Notice of Intent to Revise

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The Monograph Development—Pulmonary and Steroids Expert Committee intends to revise the Estradiol Vaginal Inserts monograph based on comments received indicating that the current procedures and acceptance criteria for impurity limits do not reflect those for a lower dose formulation contained in a recently approved ANDA.

It is proposed to revise the following:

Thin-Layer Chromatographic Identification test

1. Change the estradiol concentration in the sample solution from 2.5 mg/mL to 1.0–2.5 mg/mL.

Assay

2. Revise the Estrone standard stock solution concentration from 0.4 mg/mL to 0.1 mg/mL.
3. Revise the estrone concentration in the system suitability solution from 0.8 ?g/mL to 0.6 ?g/mL.
4. Revise the sample solution concentration from 2.5 ?g/mL to 1.0–2.5 ?g/mL.

Dissolution

1. Revise the standard solution preparation to include concentrations for both the 0.025 and 0.01 mg formulations.
2. Correct the packing of the HPLC column from 4.0–?m to 5.0–?m.
3. Correct the formula for calculating the amount of estradiol dissolved.

Organic Impurities

1. Change the concentration of estradiol in the sample solution from100 ?g/mL to 40–100 ?g/mL.
2. Change the relative retention time of Related Compound C in Table 1 from 0.74 to 0.71.
3. Add Impurity Table 2 to include acceptance criteria for the 0.01 mg/insert formulation. The impurity limits will be as follows: Estradiol Related Compound C= NMT 1.5%, Estradiol Related Compound B = NMT 1.3%, Any other individual impurity NMT 1.3%.
4. The total impurities limit for the 0.01 mg formulation will be NMT 4.0%.

It is anticipated that the proposal will be processed using an appropriate revision vehicle and the corresponding official date for the revised monograph will be indicated.

Should you have questions, please contact Domenick Vicchio, Ph.D. (301-998-6828 or dwv@usp.org).