

**Ethinyl estradiol standard stock solution**—Dissolve an accurately weighed quantity of USP Ethinyl Estradiol RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution having a known concentration of about 0.25 mg per mL.

**Desogestrel diluted standard solution**—Transfer 1.0 mL of *Desogestrel standard stock solution* to a 50-mL volumetric flask. Dilute with *Medium* to volume, and mix. This solution contains about 0.005 mg per mL of USP Desogestrel RS.

**Ethinyl estradiol diluted standard solution**—Transfer 1.0 mL of *Ethinyl estradiol standard stock solution* to a 50-mL volumetric flask. Dilute with *Medium* to volume, and mix. This solution contains about 0.005 mg per mL of USP Ethinyl Estradiol RS.

**Standard solution**—Dilute quantitative portions of *Desogestrel diluted standard solution* and *Ethinyl estradiol diluted standard solution* with *Medium* to obtain a solution containing about 0.3 µg per mL and 0.06 µg per mL of USP Desogestrel RS and USP Ethinyl Estradiol RS, respectively.

**Test solution**—Centrifuge a portion of the dissolution sample, and use the clear supernatant.

**Chromatographic system** (see *Chromatography* (621))—The liquid chromatograph is equipped with a 210-nm detector (for desogestrel analysis); a spectrofluorometric detector (for ethinyl estradiol analysis) with an excitation wavelength of 285 nm and an emission wavelength of 310 nm; a 4.6-mm × 15-cm column that contains packing L11; and a 4.6-mm × 12.5-mm guard column that also contains packing L11. The flow rate is about 2 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure*: the relative retention times are about 0.2 for ethinyl estradiol and 1.0 for desogestrel, and the relative standard deviation is not more than 3.0%.

**Procedure**—Separately inject equal volumes (about 200 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of C<sub>22</sub>H<sub>30</sub>O and C<sub>20</sub>H<sub>24</sub>O<sub>2</sub> dissolved by the formula:

$$(0.5C)(100/K)(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Desogestrel RS or USP Ethinyl Estradiol RS in the *Standard solution*; K is the labeled amount, in mg per Tablet, of C<sub>22</sub>H<sub>30</sub>O or C<sub>20</sub>H<sub>24</sub>O<sub>2</sub>; and r<sub>U</sub> and r<sub>S</sub> are the peak responses for desogestrel or ethinyl estradiol obtained from the *Test solution* and the *Standard solution*, respectively.

**Tolerances**—Not less than 80% (Q) of each of the labeled amounts of C<sub>22</sub>H<sub>30</sub>O and C<sub>20</sub>H<sub>24</sub>O<sub>2</sub> is dissolved in 30 minutes.

**TEST 2**—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

**Medium**: 0.3% sodium lauryl sulfate; 500 mL.

**Apparatus 2**: 100 rpm.

**Time**: 30 minutes.

Determine the amounts of desogestrel (C<sub>22</sub>H<sub>30</sub>O) and ethinyl estradiol (C<sub>20</sub>H<sub>24</sub>O<sub>2</sub>) dissolved by the chromatographic method used in *Test 1*.

**Tolerances**—Not less than 80% (Q) of each of the labeled amounts of C<sub>22</sub>H<sub>30</sub>O and C<sub>20</sub>H<sub>24</sub>O<sub>2</sub> is dissolved in 30 minutes.

**Uniformity of dosage units** (905): meet the requirements for *Content Uniformity* with respect to desogestrel and to ethinyl estradiol.

#### Assay—

**Mobile phase**—Prepare a filtered and degassed mixture of acetonitrile and 20 mM potassium phosphate buffer, pH 6.0 (50:50). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

**Diluent**—Prepare a mixture of acetonitrile and water (50:50).

**Desogestrel standard stock solution**—Dissolve an accurately weighed quantity of USP Desogestrel RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to

obtain a solution having a known concentration of about 0.3 mg per mL.

**Ethinyl estradiol standard stock solution**—Dissolve an accurately weighed quantity of USP Ethinyl Estradiol RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution having a known concentration of about 0.3 mg per mL.

**Standard preparation**—Dilute appropriate aliquots of *Desogestrel standard stock solution* and *Ethinyl estradiol standard stock solution* with *Diluent* to obtain a solution having a known concentration of about 0.6 µg per mL and 0.12 µg per mL of USP Desogestrel RS and USP Ethinyl Estradiol RS, respectively.

**Assay preparation**—Transfer 20 Tablets into a 200-mL volumetric flask. Add about 120 mL of *Diluent*, and shake for about 30 minutes. Dilute with *Diluent* to volume, and mix. Centrifuge a portion of the sample, and transfer an accurately measured volume to a 50-mL volumetric flask to obtain a final concentration of about 0.6 µg per mL of desogestrel. Dilute with *Diluent* to volume, and mix.

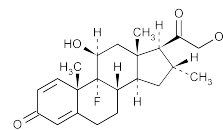
**Chromatographic system** (see *Chromatography* (621))—The liquid chromatograph is equipped with a 210-nm detector (for desogestrel analysis); a spectrofluorometric detector (for ethinyl estradiol analysis) with an excitation wavelength of 285 nm and an emission wavelength of 310 nm; a 4.6-mm × 15-cm column that contains packing L11; and a 4.6-mm × 12.5-mm guard column that also contains packing L11. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative retention times are about 0.2 for ethinyl estradiol and 1.0 for desogestrel; the tailing factor for both analytes is not more than 2.0; and the relative standard deviation is not more than 2.0%.

**Procedure**—Separately inject equal volumes (about 200 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of desogestrel (C<sub>22</sub>H<sub>30</sub>O) and ethinyl estradiol (C<sub>20</sub>H<sub>24</sub>O<sub>2</sub>) in the portion of Tablets taken by the formula:

$$100(C_S/C_U)(r_U / r_S)$$

in which C<sub>S</sub> is the concentration, in mg per mL, of USP Desogestrel RS or USP Ethinyl Estradiol RS in the *Standard preparation*; C<sub>U</sub> is the concentration, in mg per mL, of desogestrel or ethinyl estradiol in the *Assay preparation* based on the label claim; and r<sub>U</sub> and r<sub>S</sub> are the peak responses for desogestrel or ethinyl estradiol obtained from the *Assay preparation* and the *Standard preparation*, respectively.

## Desoximetasone



C<sub>22</sub>H<sub>29</sub>FO<sub>4</sub> 376.46

Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16-methyl-, (11β,16α)-.

9-Fluoro-11β,21-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione [382-67-2].

» Desoximetasone contains not less than 97.0 percent and not more than 103.0 per cent of C<sub>22</sub>H<sub>29</sub>FO<sub>4</sub>, calculated on the dried basis.

**Packaging and storage**—Preserve in well-closed containers.

**USP Reference standards** (11)—  
USP Desoximetasone RS

**Identification—**

**A:** *Infrared Absorption* (197K).

**B:** Prepare a solution of it in a mixture of chloroform and alcohol (3:1) containing 10 mg per mL. Prepare a solution of USP Desoximetasone RS in the same mixture, containing 10 mg per mL. Apply separately 20  $\mu$ L of each solution to a thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a saturated chamber containing a mixture of chloroform and ethyl acetate (1:1). Allow the solvent front to move 10 cm beyond the application point. After drying, examine the plate under UV light at 254 nm. Spray the dried plate with a 1 in 5 solution of *p*-toluenesulfonic acid in alcohol. The major spot from the test solution corresponds in value (about 0.25) and appearance to that obtained from the Standard solution.

**Melting range** (741): between 206° and 218°, but the range between beginning and end of melting does not exceed 4°.

**Specific rotation** (781S): between +107° and +112°.

*Test solution:* 5 mg per mL, in chloroform.

**Loss on drying** (731)—Dry it at 105° to constant weight: it loses not more than 1.0% of its weight.

**Residue on ignition** (281): not more than 0.2%.

**Heavy metals, Method II** (231): 0.002%.

**Assay—**

**Mobile phase**—Prepare a suitable filtered and degassed solution of methanol, water, and glacial acetic acid (65:35:1), such that the retention time of desoximetasone is about 6 minutes.

**Standard preparation**—On the day of use, weigh accurately about 20 mg of USP Desoximetasone RS, and dissolve in methanol to obtain 50.0 mL. Dilute 10.0 mL of this solution with a mixture of methanol and acetonitrile (1:1) to 100.0 mL.

**Assay preparation**—Weigh accurately 40 mg of Desoximetasone, dissolve in 100.0 mL of methanol, and proceed as directed for *Standard preparation*, beginning with "Dilute 10.0 mL of this solution."

**Procedure**—Using an injection loop, inject 10- $\mu$ L portions of the *Assay preparation* and the *Standard preparation* into a high-pressure liquid chromatograph equipped with an UV detector capable of monitoring absorption at 254 nm. The instrument is equipped with a 4.6-mm  $\times$  15-cm stainless steel column that contains packing L7 and is operated at a flow rate of about 1 mL per minute. In a suitable chromatogram, five replicate injections of the *Standard preparation* show a relative standard deviation of not more than 2.0%, and the tailing factor is not more than 1.5. Calculate the quantity, in mg, of  $C_{22}H_{29}FO_4$  in the portion of Desoximetasone taken by the formula:

$$1000C(H_U / H_S)$$

in which *C* is the concentration, in mg per mL, of USP Desoximetasone RS in the *Standard preparation*, and  $H_U$  and  $H_S$  are the peak heights of desoximetasone obtained from the *Assay preparation* and the *Standard preparation*, respectively.

**Desoximetasone Cream**

» Desoximetasone Cream is Desoximetasone in an emollient cream base. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of  $C_{22}H_{29}FO_4$ .

**Packaging and storage**—Preserve in collapsible tubes, at controlled room temperature.

**USP Reference standards (11)—**

USP Desoximetasone RS

**Identification**—Evaporate 25 mL of the *Assay preparation*, prepared as directed in the *Assay*, on a steam bath just to dryness, and dissolve the residue in 2 mL of acetonitrile. This is the test solution. Prepare a Standard solution of USP Desoximetasone RS in acetonitrile containing 500  $\mu$ g per mL. Using 10  $\mu$ L instead of 20  $\mu$ L of each solution, proceed as directed in *Identification test B* under *Desoximetasone*, beginning with "Apply separately 20  $\mu$ L of each." The specified result is observed.

**Minimum fill** (755): meets the requirements.

**pH** (791): between 4.0 and 8.0, in a solution prepared in the following manner. Add 15 mL of boiling water to 3.5 g of the Cream in a 50-mL centrifuge tube, cap the tube, shake vigorously until the cream is uniformly dispersed, then place the tube in a steam bath until the water and oil layers separate completely. Cool, separate the layers, and determine the pH of the aqueous phase.

**Assay—**

**Mobile phase**—Prepare a filtered and degassed mixture of methanol, water, and glacial acetic acid (65:35:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

**Internal standard solution**—Prepare a solution of ethylparaben in methanol having a concentration of about 0.04 mg per mL.

**Standard preparation**—Dissolve an accurately weighed quantity of USP Desoximetasone RS in methanol to obtain a solution having a known concentration of about 0.4 mg per mL. Pipet 5 mL of this solution into a 50-mL centrifuge tube. Add 10.0 mL of *Internal standard solution*, dilute with methanol quantitatively to 40.0 mL, and mix to obtain the *Standard preparation* having a known concentration of about 0.05 mg per mL.

**Assay preparation**—Transfer an accurately weighed amount of Cream, equivalent to about 2 mg of desoximetasone, to a 50-mL centrifuge tube, and add a few 3-mm glass beads. Add 10.0 mL of *Internal standard solution* and about 30 mL of methanol, and mix. Tightly cap the centrifuge tube, and immerse it for 10 minutes in a bath maintained at a temperature of 65°. Remove the tube from the bath, and immediately vortex at high speed for 30 seconds. Return the tube to the hot water bath for 5 minutes, remove it from the bath, and immediately vortex for 30 seconds. Repeat the procedure one more time, then cool the tube in an ice-bath held at 10° until no further flocculent precipitation occurs. Centrifuge, and use the supernatant.

**Chromatographic system** (see *Chromatography* (621))—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm  $\times$  15-cm column that contains packing L7. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative retention times are about 1 and 2 for ethylparaben and desoximetasone, respectively; the tailing factor for the analyte peak is not more than 2.0; the resolution,  $R_s$ , between the analyte and internal standard peaks is not less than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

**Procedure**—Separately inject equal volumes (about 10  $\mu$ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of  $C_{22}H_{29}FO_4$  in the portion of Cream taken by the formula:

$$40C(R_U/R_S)$$

in which *C* is the concentration, in mg per mL, of USP Desoximetasone RS in the *Standard preparation*; and  $R_U$  and  $R_S$  are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.