

BRIEFING

Mifepristone. This monograph has been posted on the USP Pending Standards Web page for review and public comment for more than 90 days. No comments were received. The Monograph Development—Pulmonary and Steroids Expert Committee reviewed the proposed monograph, and approved it as an Authorized USP Pending Standard with the following changes in the test for *Related compounds*.

1. The subsection heading “0.05 M Phosphate buffer” has been changed to “0.05 M Phosphate solution,” because the solution is not a buffer.
2. Under the *Chromatographic system*, it is clarified that the detector is set at 250 nm.
3. “Peak responses” has been changed to “peak areas” to clarify that peak areas are used.
4. The chemical names provided for the impurities listed in *Table I* have been corrected.

The liquid chromatographic test for *Related compounds* is based on analyses performed with the Suplex PKB100 brand of L68 column. The typical retention time for mifepristone is about 20 minutes.

An authorized version of this monograph was posted on the USP Website on Aug. 29, 2008. The following corrections are made:

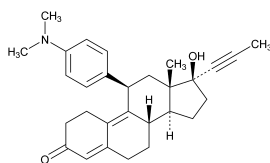
1. The chemical structure of Mifepristone is replaced to correct the stereochemical configuration on Carbon 17.
2. The first listed chemical name for Mifepristone is revised to be consistent with the USP-NF naming convention.

(MD-PS: D. Bempong) RTS—C48849

Add the following:

► **Mifepristone**

v. 1.1 Authorized September 1, 2008



C₂₉H₃₅NO₂ 429.59

Estra-4,9-dien-3-one, 11β-[4-(dimethylamino)phenyl]-17β-hydroxy-17α-(prop-1-ynyl)-.

11β-[p-(Dimethylamino)phenyl]-17β-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one. [84371-65-3].

» Mifepristone contains not less than 97.0 percent and not more than 103.0 percent of C₂₉H₃₅NO₂, calculated on the anhydrous, solvent-free basis.

Packaging and storage—Preserve in well-closed containers, and store at room temperature.

USP Reference standards (11)—*USP Mifepristone RS*.

Identification—

A: *Infrared Absorption* (197K).

B: The retention time of the major peak in the chromatogram of the *Test solution* corresponds to that in the chromatogram of the *Standard identification solution*, as obtained in the test for *Related compounds*.

Specific rotation (781S): between +124° and +135°.

Test solution: 5 mg per mL, in methylene chloride at 20°.

Water, Method I (921): not more than 0.5%.

Residue on ignition (281): not more than 0.5%.

Heavy metals, Method I (231): not more than 20 ppm.

Related compounds—

0.05 M Phosphate solution—Dissolve 7.80 g of monobasic sodium phosphate with water, and dilute with water to 1 L.

Mobile phase—Prepare a filtered and degassed mixture of *0.05 M Phosphate solution* and acetonitrile (55:45). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

Standard solution—Dissolve an accurately weighed quantity of USP Mifepristone RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 5 µg per mL.

Standard identification solution—Dissolve an accurately weighed quantity of USP Mifepristone RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 1 mg per mL.

System sensitivity solution—Transfer 1 mL of the *Standard solution* into a 10-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

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Test solution—Transfer about 10 mg of Mifepristone, accurately weighed, to a 10-mL volumetric flask, dissolve in *Mobile phase*, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with a detector set at 250 nm, and a 4.6-mm × 25-cm column that contains 5-μm packing L68. The flow rate is about 1.2 mL per minute. Chromatograph the *System sensitivity solution*, and calculate the signal-to-noise ratio, S/N, for the mifepristone peak by the formula:

$$(2H)/h$$

in which H is the measured height of the mifepristone peak, and h is the amplitude of the average measured baseline noise. The S/N is not less than 10. Chromatograph the *Standard solution*, and record the peak areas as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 10%.

Procedure—Separately inject equal volumes (about 20 μL) of the *Standard solution*, the *Test solution*, and the *Standard identification solution* into the chromatograph, record the

chromatograms for at least two times the retention time of mifepristone, and measure the peak areas. Calculate the percentage of each impurity in the portion of Mifepristone taken by the formula:

$$100(1/F)(C_s/C_T)(r_i/r_s)$$

in which F is the relative response factor (see *Table 1* for values); C_s is the concentration, in mg per mL, of mifepristone in the *Standard solution*; C_T is the concentration, in mg per mL, of mifepristone in the *Test solution*; r_i is the peak area of the individual impurity in the *Test solution*; and r_s is the peak area of mifepristone in the *Standard solution*. The limits are as provided in *Table 1*. [NOTE—The *Standard identification solution* is injected for identification purposes only. See *Identification test B*.]

Assay—Dissolve about 750 mg of Mifepristone, accurately weighed, in 50 mL of glacial acetic acid. Add 5 drops of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a blue endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 42.96 mg of $C_{29}H_{35}NO_2$. ◀ (1-Sep-2008)

Table 1

Compound	Relative Retention Time	Relative Response Factor	Limit (%)
Demethylated derivative ^a	0.62	1.0	0.5
Ethylene-ani-pynyelone ^b	0.77	0.6	0.10
11 α -isomer of mifepristone ^c	0.88	1.0	0.10
Mifepristone	1.00	—	—
Individual unknown impurity	—	1.0	0.10
Total impurities	—	—	1.0

^a 11 β -[*p*-(Methylamino)phenyl]-17 β -hydroxy-17-(1-propynyl)estra-4,9-dien-3-one.

^b 3, 3-(Ethylenedioxy)-5 α -hydroxy-11 β -[*p*-(dimethylamino)phenyl]-17 β -hydroxy-17-(1-propynyl)estra-9-en.

^c 11 α -[*p*-(Dimethylamino)phenyl]-17 β -hydroxy-17-(1-propynyl)estra-4,9-dien-3-one.