

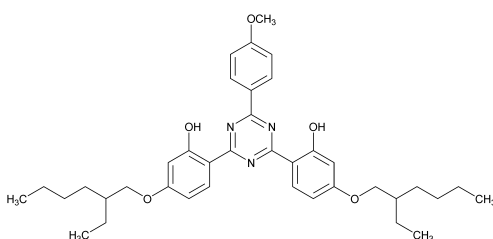
BRIEFING

**Bemotrizinol.** The revision of this monograph was posted on the USP Website as a draft USP Pending Monograph for public comment on July 25, 2008. No comments were received. The MD-OD Expert Committee reviewed the draft and approved the monograph as an Authorized USP Pending Monograph.

(MD-OD: F. Mao) RTS—C59051

**Bemotrizinol**

v.2 Authorized February 1, 2009



C<sub>38</sub>H<sub>49</sub>N<sub>3</sub>O<sub>5</sub> 627.80  
Phenol, 2,2'-[6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]].  
2,2'-[6-(4-Methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]phenol] [CAS-187393-00-6].

» Bemotrizinol contains not less than 96.5 percent and not more than 100.0 percent of C<sub>38</sub>H<sub>49</sub>N<sub>3</sub>O<sub>5</sub>, calculated on the as-is basis.

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

**USP Reference standards** (11)—USP Bemotrizinol RS. USP Bemotrizinol Impurity Mixture RS.

**Identification**—

**A:** Ultraviolet Absorption (197U)—

Spectral range: 210 to 750 nm.

Solution: 10 µg per mL.

Medium: 1,4-dioxane.

Ratio: A<sub>308</sub>/A<sub>342</sub> is about 0.9.

**B:** The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation, as obtained in the Assay.

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

**Related compounds**—

Diluent, Buffer, Solution A, Solution B, and Mobile phase—Proceed as directed in the Assay.

**Test solution**—Dissolve a known quantity of Bemotrizinol in 1,4-dioxane, and sonicate if necessary, to obtain a solution having a concentration of about 5.0 mg per mL. Further dilute this solution with Diluent to obtain a solution having a concentration of about 1.0 mg per mL.

**Peak identification solution**—Prepare a solution of USP Bemotrizinol Impurity Mixture RS, in the exact same manner as for the Test solution, containing about 1.0 mg of the USP Bemotrizinol Impurity Mixture RS per mL.

**Standard stock solution**—Transfer about 25 mg of USP Bemotrizinol RS, accurately weighed, to a 100-mL volumetric flask. Dissolve by sonication for 5 minutes in 60 mL of 1,4-dioxane. Cool to room temperature, dilute with 1,4-dioxane to volume, and mix.

**Standard solution**—Pipet 2.0 mL of the Standard stock solution into a 50-mL volumetric flask, dilute with Diluent to volume, and mix to obtain a solution having a known concentration of 10 µg per mL.

**Sensitivity check solution**—Pipet 2.0 mL of the Standard stock solution into a 50-mL volumetric flask, dilute with 1,4-dioxane to volume, and mix. Pipet 5.0 mL of this solution into a 100-mL volumetric flask, dilute with Diluent to volume, and mix to obtain a solution having a concentration of 0.5 µg per mL.

**Chromatographic system** (see Chromatography (621))—Proceed as directed in the Assay. In addition, chromatograph the Peak identification solution, and record the peak responses as directed for Procedure: identify the impurity peaks by the relative retention times listed in Table 1. Chromatograph the Sensitivity check solution, and calculate the signal-to-noise ratio (S/N) by the formula:

$$(2H)/h$$

in which *H* is the measured height of the bemotrizinol peak; and *h* is the amplitude of the average measured baseline noise: the S/N is not less than 10.

**Procedure**—Separately inject a volume (about 20 µL) of the Test solution, the Standard solution, and the Sensitivity check solution into the chromatograph; record the chromatograms; measure the peak responses of bemotrizinol in the Standard solution, the Test solution, and the Sensitivity check solution; and measure the response of any impurity peak in the Test solution with a response greater than that obtained for bemotrizinol in the Sensitivity check solution. Calculate the percentage of each impurity in the portion of Bemotrizinol taken by the formula:

$$50(C/FW)(r_i/r_U)$$

in which *C* is the concentration, in µg per mL, of USP Bemotrizinol RS in the Standard solution; *F* is the relative response factor for each impurity obtained (see Table 1); *W* is the weight, in mg, of Bemotrizinol taken; *r<sub>i</sub>* is the peak response for each individual impurity in the Test solution with a response equal to or greater than the bemotrizinol peak obtained from the Sensitivity check solution; and *r<sub>U</sub>* is the response of the bemotrizinol peak obtained from the Test solution. The limits are shown in Table 1.

**Assay**—

**Diluent**—Prepare a mixture containing 1,4-dioxane and water (80:20).

**Buffer**—Transfer 600 mg of ammonium formate to a 1000-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Adjust with formic acid to a pH of 4.6.

**Solution A**—Use the Buffer; filtered and degassed.

**Solution B**—Use 1,4-dioxane.

**Mobile phase**—Use variable mixtures of Solution A and Solution B as directed for Chromatographic system. Make adjustments if necessary (see System Suitability under Chromatography (621)).

**Standard preparation**—Transfer about 50 mg of USP Bemotrizinol RS, accurately weighed, to a 50-mL volumetric flask. Dissolve by sonication in 40 mL of 1,4-dioxane. Cool to room temperature, dilute with 1,4-dioxane to volume, and mix. Pipet 5.0 mL of this solution into a 50-mL volumetric flask, and dilute with Diluent to volume.

**Assay preparation**—Transfer about 50 mg of Bemotrizinol, accurately weighed, to a 50-mL volumetric flask. Dissolve by sonication in 40 mL of 1,4-dioxane. Cool to room temperature, dilute with 1,4-dioxane to volume, and mix. Pipet 5.0 mL of this solution into a 50-mL volumetric flask, and dilute with Diluent to volume.

**Chromatographic system** (see Chromatography (621))—The liquid chromatograph is equipped with a 332-nm detector and a 3.0-mm × 12.5-cm column that contains packing L1. The flow rate is about 0.3 mL per minute. The column temperature is maintained at 35°. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0–5	20	80	isocratic
5–25	20→0	80→100	linear gradient
25–27	0	100	isocratic
27–27.1	0→20	100→80	linear gradient
27.1–38	20	80	isocratic

Table 1

Compound Name	Relative Retention Time	Relative Response Factor (F)	Limit (%)
2-[2-Hydroxy-4-(2-ethylhexyloxy)phenyl]-4-(resorcinol-4-yl)-6-(4-methoxyphenyl)-1,3,5-triazine	0.26	1.1	1.0
4-(2-Ethylhexyloxy)-2-hydroxybenzophenone	0.30	0.40	1.0
Impurity A	0.35	1.1	1.0
2-[4-(2-Ethylhexyloxy)-2-hydroxyphenyl]-4,6-bis(4-methoxyphenyl)-1,3,5-triazine	0.39	1.1	1.0
Bemotrizinol	1.00	—	—
2-[2,4-Bis(2-ethylhexyloxy)phenyl]-4-[2-hydroxy-4-(2-ethylhexyloxy)phenyl]-6-(4-methoxyphenyl)-1,3,5-triazine	1.46	0.77	1.0
Impurity B	1.62	0.77	1.0
2,4,6-Tris[2-hydroxy-4-(2-ethylhexyloxy)phenyl]-1,3,5-triazine	1.66	0.67	1.0
2,4-Bis[2-hydroxy-4-(2-ethylhexyloxy)phenyl]-6-[4-(2-ethylhexyloxy)phenyl]-1,3,5-triazine	1.69	0.83	1.0
Any other unknown impurity	—	1.0	0.1
Total impurities	—	—	<2.5

Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative standard deviation for replicate injections of the *Standard preparation* is not more than 1.0%.

*Procedure*—Separately inject equal volumes (about 10 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 quantity, in mg, of  $C_{38}H_{49}N_3O_5$  in the portion of Bemotrizinol taken by the formula:

$$500C(r_U/r_S)$$

in which  $C$  is the concentration, in mg per mL, of USP Bemotrizinol RS in the *Standard preparation*; and  $r_U$  and  $r_S$  are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.