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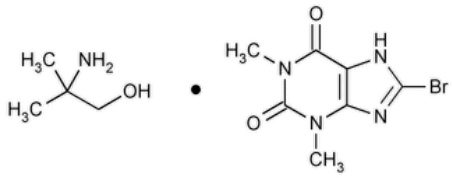
Pamabrom



$C_{11}H_{18}BrN_5O_3$ 348.20

8-Bromo-3,7-dihydro-1,3-dimethyl-1-*H*-purine-2,6-dione compound with 2-amino-2-methyl-1-propanol (1:1).

8-Bromotheophylline compound with 2-amino-2-methyl-1-propanol (1:1) CAS RN®: 606-04-02.

» Pamabrom contains not less than 72.2 percent and not more than 76.6 percent of 8-bromotheophylline ($C_7H_7BrN_4O_2$), calculated on the anhydrous basis; and not less than 24.6 percent and not more than 26.6 percent of 2-amino-2-methyl-1-propanol ($C_4H_{11}NO$), calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—

USP 8-Bromotheophylline RS

8-Bromo-3,7-dihydro-1,3-dimethyl-1*H*-purine-2,6-dione.

$C_7H_7N_4O_2Br$ 259.06

USP Theophylline RS

Identification—It responds to the *Thin-layer Chromatographic Identification Test* ⟨201⟩, using a solvent system consisting of a mixture of xylene, methanol, and glacial acetic acid (11:2:1) and a *Standard solution* and a *Test solution* prepared as directed below: the R_F value of the principal spot, which appears as a dark spot against a green background, from the *Test solution* corresponds to that obtained from the *Standard solution*.

Standard solution—Transfer an accurately weighed quantity of about 20 mg of USP 8-Bromotheophylline RS to a 100-mL volumetric flask, add 25 mL of water, 50 mL of methanol, and a small amount of dilute ammonium hydroxide. Swirl the flask to effect solution. Dilute the contents of the flask with methanol to volume, and mix.

Test solution—Transfer an accurately weighed quantity of about 25 mg of Pamabrom to a 100-mL volumetric flask, add 25 mL of water, and swirl to dissolve. Dilute the contents of the flask with methanol to volume, and mix.

Water Determination, *Method I* ⟨921⟩: not more than 3%.

Limit of theophylline—

Diluting solution, Mobile phase, and *Chromatographic system*—Proceed as directed in the *Assay for 8-bromotheophylline.*

Standard solution—Dissolve an accurately weighed quantity of USP Theophylline RS in *Diluting solution*, add a few drops of ammonium hydroxide, sonicating if necessary, to obtain a solution having a known concentration of about 1 mg of USP Theophylline RS per mL. Dilute a volume of this solution quantitatively, and stepwise if necessary, with *Diluting solution* to obtain a solution having a known concentration of about 5 µg per mL.

Test solution—Transfer an accurately weighed quantity of about 200 mg of Pamabrom to a 200-mL volumetric flask. Add about 50 mL of *Diluting solution*, and sonicate for 5 minutes. Cool to room temperature, dilute with *Diluting solution* to volume, and mix.

Procedure—Separately inject equal volumes (about 20 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 theophylline in the portion of Pamabrom taken by the formula:

$$20(C/W)(r_U/r_S)$$

in which C is the concentration, in µg per mL, of USP Theophylline RS in the *Standard solution*, W is the weight, in mg, of Pamabrom taken, and r_U and r_S are the peak responses of theophylline obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.5% is found.

Assay for 8-bromotheophylline—

Diluting solution—Prepare a mixture of water and methanol (70:30).

Mobile phase—Prepare a filtered and degassed mixture of water, methanol, and glacial acetic acid (69:30:1), filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Internal standard solution—Dissolve an accurately weighed quantity of caffeine in *Diluting solution*, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a concentration of about 125 µg of caffeine per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP 8-Bromotheophylline RS in *Diluting solution*, add a few drops of ammonium hydroxide, sonicating if necessary, to obtain a solution having a known concentration of about 0.75 mg of USP 8-Bromotheophylline RS per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, add 10.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, mix, and filter.

Assay preparation—Transfer an accurately weighed quantity of about 200 mg of Pamabrom to a 200-mL volumetric flask, add about 50 mL of *Diluting solution* and two drops of ammonium hydroxide, and sonicate for 5 minutes. [NOTE—If a hazy solution is present after 5 minutes of sonication, add 1 additional drop of ammonium hydroxide.] Cool, dilute with *Diluting solution* to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, add 10.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, mix, and filter.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 15-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph 20 µL of the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative retention times are about 0.6 for caffeine and 1.0 for 8-bromotheophylline, the resolution, *R,* between caffeine and 8-bromotheophylline 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 20 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 8-bromotheophylline ($C_7H_7BrN_4O_2$) in the portion of Pamabrom taken by the formula:

$$4000C(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP 8-Bromotheophylline RS in the *Standard preparation*, and R_U and R_S are the peak response ratios of the 8-bromotheophylline peak and the internal standard peak obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Assay for 2-amino-2-methyl-1-propanol—Dissolve about 1 g of Pamabrom, accurately weighed, in 10 mL of water by warming gently on a steam bath until the solution is clear. Cool, add methyl orange TS, and titrate with 0.5 N hydrochloric acid VS. Perform a blank determination, and make any necessary correction (see *Titrimetry ⟨541⟩*). Each mL of 0.5 N hydrochloric acid is equivalent to 44.57 mg of $C_4H_{11}NO$.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
PAMABROM	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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