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# Hydrocodone Bitartrate and Homatropine Methylbromide Tablets

## DEFINITION

Hydrocodone Bitartrate and Homatropine Methylbromide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of hydrocodone bitartrate disesquihydrate ( $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2\frac{1}{2}H_2O$ ) and homatropine methylbromide ( $C_{17}H_{24}BrNO_3$ ).

[NOTE—Use of silanized autosampler vials such as dimethyldichlorosilane vials<sup>1</sup> is required for *Dissolution Test 1* and *Test 2*, the *Limit* tests, and the *Assay* to prevent drug degradation.]

## IDENTIFICATION

- **A.** The UV absorption spectra of the hydrocodone bitartrate and homatropine methylbromide peaks of the *Sample solution* and those of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the *Assay*.
- **B.** The retention times of the hydrocodone bitartrate and homatropine methylbromide peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

## ASSAY

**Change to read:**

### • PROCEDURE

**Buffer:** 0.005 M dibasic potassium phosphate. Adjust with phosphoric acid to a pH of  $6.4 \pm 0.1$ ▲ (ERR 1-Jul-2022) .

**Mobile phase:** Acetonitrile and *Buffer* (30:170)

**Standard solution:** 0.2 mg/mL of [USP Hydrocodone Bitartrate RS](#) and 0.06 mg/mL of [USP Homatropine Methylbromide RS](#) in *Mobile phase*

**Sample solution:** Nominally 0.2 mg/mL of hydrocodone bitartrate and 0.06 mg/mL of homatropine methylbromide prepared as follows.

Transfer a portion of fine powder from NLT 20 Tablets to a suitable volumetric flask. Add 60% of the final volume of *Mobile phase*, sonicate for 15 min, and then shake with a wrist-action shaker for an additional 15 min. Dilute with *Mobile phase* to volume. Pass the solution through a suitable filter of 0.45-μm pore size.

### Chromatographic system

**Mode:** LC

#### Detectors

**Assay:** UV 230 nm

**Identification test A:** Diode array, UV 200–400 nm

**Column:** 4.6-mm × 25-cm; 5-μm packing L7

**Flow rate:** 1.5 mL/min

**Injection volume:** 10 μL

### System suitability

**Sample:** *Standard solution*

[NOTE—The relative retention times for homatropine methylbromide and hydrocodone bitartrate are about 0.44 and 1.0, respectively.]

### Suitability requirements

**Resolution:** NLT 2.5 between hydrocodone bitartrate and homatropine methylbromide

**Relative standard deviation:** NMT 3.0% for each analyte

### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of homatropine methylbromide ( $C_{17}H_{24}BrNO_3$ ) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$  = peak response of homatropine methylbromide from the *Sample solution*

$r_S$  = peak response of homatropine methylbromide from the *Standard solution*

$C_s$  = concentration of [USP Homatropine Methylbromide RS](#) in the *Standard solution* (mg/mL)

$C_u$  = nominal concentration of homatropine methylbromide in the *Sample solution* (mg/mL)

Calculate the percentage of the labeled amount of hydrocodone bitartrate disesquihydrate ( $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2\frac{1}{2}H_2O$ ) in the portion of Tablets taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (M_{r1}/M_{r2}) \times 100$$

$r_u$  = peak response of hydrocodone bitartrate from the *Sample solution*

$r_s$  = peak response of hydrocodone bitartrate from the *Standard solution*

$C_s$  = concentration of [USP Hydrocodone Bitartrate RS](#) in the *Standard solution* (mg/mL)

$C_u$  = nominal concentration of hydrocodone bitartrate in the *Sample solution* (mg/mL)

$M_{r1}$  = molecular weight of hydrocodone bitartrate disesquihydrate, 494.49

$M_{r2}$  = molecular weight of anhydrous hydrocodone bitartrate, 449.46

**Acceptance criteria:** 90.0%–110.0%

## PERFORMANCE TESTS

### • [DISSOLUTION \(711\)](#)

#### Test 1

**Medium:** Water; 900 mL, deaerated

**Apparatus 2:** 50 rpm

**Time:** 30 min

**Buffer and Mobile phase:** Prepare as directed in the Assay.

**Standard solution:** 0.0055 mg/mL of [USP Hydrocodone Bitartrate RS](#) and 0.00165 mg/mL of [USP Homatropine Methylbromide RS](#) in *Medium*

**Sample solution:** Pass the solution under test through a suitable filter of 0.45- $\mu$ m pore size.

**Chromatographic system:** Proceed as directed in the Assay, with the following exception.

**Injection volume:** 250  $\mu$ L

#### System suitability

**Sample:** *Standard solution*

#### Suitability requirements

**Resolution:** NLT 13 between homatropine methylbromide and hydrocodone bitartrate

**Relative standard deviation:** NMT 3.0% for each analyte

#### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of hydrocodone bitartrate disesquihydrate ( $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2\frac{1}{2}H_2O$ ) and homatropine methylbromide ( $C_{17}H_{24}BrNO_3$ ) dissolved:

$$\text{Result} = (r_u/r_s) \times C_s \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

$r_u$  = peak area of hydrocodone bitartrate or homatropine methylbromide from the *Sample solution*

$r_s$  = peak area of hydrocodone bitartrate or homatropine methylbromide from the *Standard solution*

$C_s$  = concentration of [USP Hydrocodone Bitartrate RS](#) or [USP Homatropine Methylbromide RS](#) in the *Standard solution* (mg/mL)

$V$  = volume of *Medium*, 900 mL

$L$  = label claim for each drug substance (mg/Tablet)

$M_{r1}$  = molecular weight of hydrocodone bitartrate disesquihydrate, 494.49

$M_{r2}$  = molecular weight of anhydrous hydrocodone bitartrate, 449.46