

Status: Currently Official on 15-Feb-2025
 Official Date: Official as of 01-May-2021
 Document Type: USP Monographs
 DocId: GUID-9D56DB96-41CE-4993-8C00-CCE289366497_3_en-US
 DOI: https://doi.org/10.31003/USPNF_M55170_03_01
 DOI Ref: 0ae6a

© 2025 USPC
 Do not distribute

Nadolol and Bendroflumethiazide Tablets

DEFINITION

Nadolol and Bendroflumethiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of nadolol ($C_{17}H_{27}NO_4$) and bendroflumethiazide ($C_{15}H_{14}F_3N_3O_4S_2$).

IDENTIFICATION

Change to read:

• **A.** The retention times of the two major peaks of the *Sample solution* correspond to [▲]those[▲] (USP 1-May-2021) of the *Standard solution*, [▲]as obtained[▲] (USP 1-May-2021) in the Assay.

Add the following:

▲• **B.** The UV spectra of the two major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.▲
 (USP 1-May-2021)

ASSAY

Change to read:

• PROCEDURE

[**CAUTION**—Use low-actinic glassware for the *Sample solution* and the *Standard solution*.]

Mobile phase: Transfer 5.62 g of [anhydrous sodium chloride](#) and 1.97 g of [sodium acetate](#) to 1000 mL of [water](#) in a 2-L volumetric flask. Add 4.0 mL of [glacial acetic acid](#) and 800 mL of [methanol](#). Dilute with [water](#) to volume.

System suitability solution: 0.4 mg/mL each of [USP Nadolol RS](#) and [USP 2,4-Disulfamyl-5-trifluoromethylaniline RS](#) in [methanol](#)

Standard solution: 0.4 mg/mL of [USP Nadolol RS](#) and 0.4J mg/mL of [USP Bendroflumethiazide RS](#) in [methanol](#), where J is the ratio of the labeled amount of bendroflumethiazide, in milligrams, to the labeled amount of nadolol, in mg/Tablet

Sample solution: Nominally equivalent to 0.4 mg/mL of nadolol in [methanol](#) prepared as follows. Transfer a portion of finely powdered Tablets (NLT 20), equivalent to 40 mg of nadolol, to a 100-mL volumetric flask. Add [methanol](#), and sonicate for 15 min with occasional shaking. Dilute with [methanol](#) to volume, and centrifuge.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 270 nm.▲For *Identification B*, use a diode array detector in the range of 210–400 nm.▲ (USP 1-May-2021)

Column: ▲3.9-mm▲ (USP 1-May-2021) × 30-cm; ▲10-μm▲ (USP 1-May-2021) packing [L11](#)

Flow rate: 1.5 mL/min

Injection volume: 20 μL

▲**Run time:** NLT 2 times the retention time of bendroflumethiazide▲ (USP 1-May-2021)

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for nadolol and bendroflumethiazide are about 0.3 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.4 between the solvent and 2,4-disulfamyl-5-trifluoromethylaniline peaks; NLT 1.4 between the 2,4-disulfamyl-5-trifluoromethylaniline and nadolol peaks, ▲*System suitability solution*;▲ (USP 1-May-2021) and NLT 1.7 between the nadolol and bendroflumethiazide peaks, ▲*Standard solution*▲ (USP 1-May-2021)

Relative standard deviation: NMT 3.0% ▲for the nadolol and bendroflumethiazide peaks,▲ (USP 1-May-2021) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of nadolol ($C_{17}H_{27}NO_4$) in the portion of Tablets taken:

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

r_U = peak response of nadolol from the *Sample solution*

r_S = peak response of nadolol from the *Standard solution*

C_S = concentration of [USP Nadolol RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of nadolol in the *Sample solution* (mg/mL)

Calculate the percentage of the labeled amount of bendroflumethiazide ($C_{15}H_{14}F_3N_3O_4S_2$) in the portion of Tablets taken:

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

r_U = peak response of bendroflumethiazide from the *Sample solution*

r_S = peak response of bendroflumethiazide from the *Standard solution*

C_S = concentration of [USP Bendroflumethiazide RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of bendroflumethiazide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\), Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms, Procedure for a pooled sample for immediate-release dosage forms](#)

[CAUTION—Protect solutions from light throughout this test.]

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: Dissolve [USP Nadolol RS](#) and [USP Bendroflumethiazide RS](#) in a minimal amount of [methanol](#), and dilute with *Medium* to the desired concentrations.

Sample solution: ▲ Pass a ▲ (USP 1-May-2021) portion of the solution under test ▲ through a suitable filter. ▲ (USP 1-May-2021) Dilute with *Medium* to a concentration that is similar to the *Standard solution*.

Chromatographic system and System suitability: Proceed as directed in the Assay.

▲ Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of nadolol ($C_{17}H_{27}NO_4$) or bendroflumethiazide ($C_{15}H_{14}F_3N_3O_4S_2$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times D \times V \times (1/L) \times 100$$

r_U = peak response of nadolol or bendroflumethiazide from the *Sample solution*

r_S = peak response of nadolol or bendroflumethiazide from the *Standard solution*

C_S = concentration of [USP Nadolol RS](#) or [USP Bendroflumethiazide RS](#) in the *Standard solution* (mg/mL)

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet) ▲ (USP 1-May-2021)

Tolerances: NLT 80% (Q) of the labeled amount of nadolol ($C_{17}H_{27}NO_4$) and bendroflumethiazide ($C_{15}H_{14}F_3N_3O_4S_2$) is dissolved.

- [UNIFORMITY OF DOSAGE UNITS \(905\), Content Uniformity:](#) Meet the requirements

IMPURITIES

Add the following:

▲ ORGANIC IMPURITIES, PROCEDURE 1: NADOLOL RELATED IMPURITIES

[CAUTION—Protect all solutions containing nadolol from light.]

Buffer: Transfer 3.85 g of [ammonium acetate](#) into 1000 mL of [water](#). Adjust with 5 N [hydrochloric acid](#) to a pH of 4.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (89:11)

Standard solution: 0.016 mg/mL of [USP Nadolol RS](#) in *Mobile phase*

Sensitivity solution: 0.0016 mg/mL of [USP Nadolol RS](#) from the *Standard solution* in *Mobile phase*

Sample solution: Nominally 3.2 mg/mL of nadolol prepared as follows. Transfer a suitable amount, equivalent to 160 mg of nadolol, from finely powdered Tablets (NLT 20) to a suitable volumetric flask. Add *Mobile phase* to 80% of the volume of the flask. Shake and mix for 15