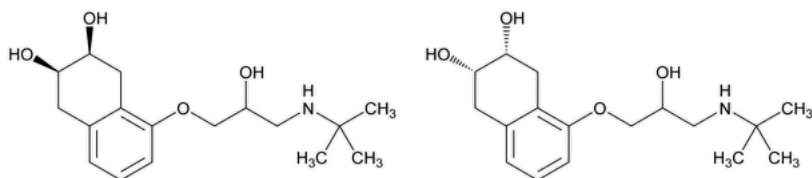


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Nadolol

Change to read:



$C_{17}H_{27}NO_4$ 309.40

2,3-Naphthalenediol, 5-[3-[(1,1-dimethylethylamino)-2-hydroxypropoxy]-1,2,3,4-tetrahydro-, *cis*;-
 1-(*tert*-Butylamino)-3-[(5,6,7,8-tetrahydro-*cis*-6,7-dihydroxy-1-naphthyl)oxy]-2-propanol;

▲(2*RS*,3*SR*)-5-[3-(*tert*-Butylamino)-2-hydroxypropoxy]-1,2,3,4-tetrahydronaphthalene-2,3-diol▲ (USP 1-Dec-2023) CAS RN®: 42200-33-9; UNII: FEN504330V.

DEFINITION

Nadolol contains NLT 98.0% and NMT 102.0% of nadolol ($C_{17}H_{27}NO_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197M ▲ or 197A▲ (USP 1-Dec-2023)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

PROCEDURE

Solution A: 0.1% ▲(v/v)▲ (USP 1-Dec-2023) [trifluoroacetic acid](#)▲ in water prepared as follows. For 1 L, add 1.0 mL of [trifluoroacetic acid](#) into 1000 mL of [water](#).▲ (USP 1-Dec-2023)

Mobile phase: [Acetonitrile](#) and *Solution A* (15:85)

Standard solution: 0.2 mg/mL of [USP Nadolol RS](#) in *Mobile phase*. Sonication and occasional hand shaking may be necessary for complete dissolution.

Sample solution: 0.2 mg/mL of Nadolol in *Mobile phase*. Sonication and occasional hand shaking may be necessary for complete dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 270 nm

Column: 4.6-mm × 15-cm; 3.5-μm packing [L1](#)

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 μL

Run time: NLT 1.7 times the retention time of nadolol ▲▲ (USP 1-Dec-2023)

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nadolol ($C_{17}H_{27}NO_4$) in the portion of Nadolol 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 = concentration of Nadolol in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

OTHER COMPONENTS

Change to read:

• RACEMATE COMPOSITION

▲ **Mobile phase:** [Hexane](#) and [alcohol, dehydrated](#) (86:14). For 1 L, add 0.3 mL each of [diethylamine](#) and [glacial acetic acid](#) into each liter of the mixture.

Standard solution: 0.2 mg/mL of [USP Nadolol RS](#) in [alcohol, dehydrated](#)

Sample solution: 0.2 mg/mL of Nadolol in [alcohol, dehydrated](#)

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 2.1-mm × 15-cm; 3-μm packing [L40](#)

Flow rate: 0.2 mL/min

Injection volume: 2 μL

Run time: NLT 2.4 times the retention time of the last eluted isomer

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for the four isomers are 0.48, 0.54, 0.84, and 1.0, respectively. The first and last eluted are isomers of nadolol racemate A while the second and third eluted are isomers of nadolol racemate B.]

Suitability requirements

Resolution: NLT 1.0 between the first and the second eluted isomers.

Relative standard deviation: NMT 5.0% for the ratios between the sum of peak responses of isomers of racemate A and the sum of peak responses of isomers of racemate B.

Analysis

Sample: *Sample solution*

Calculate the percentage of racemate A in the portion of Nadolol taken:

$$\text{Result} = r_A / (r_A + r_B) \times 100$$

r_A = sum of peak responses of isomers of nadolol racemate A

r_B = sum of peak responses of isomers of nadolol racemate B

▲ (USP 1-Dec-2023)

Acceptance criteria: 40%–60%

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.1%

Change to read:

• ORGANIC IMPURITIES

Solution A: Prepare as directed in the Assay.

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
3	85	15