

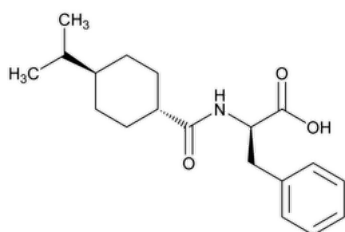
Status: Currently Official on 15-Feb-2025  
 Official Date: Official as of 01-Nov-2020  
 Document Type: USP Monographs  
 DocId: GUID-C241B9A3-6481-4688-854B-22A5404BA469\_5\_en-US  
 DOI: [https://doi.org/10.31003/USPNF\\_M2883\\_05\\_01](https://doi.org/10.31003/USPNF_M2883_05_01)  
 DOI Ref: ma22z

© 2025 USPC  
 Do not distribute

# Nateglinide

**Change to read:**

▲



▲ (ERR 1-Nov-2020)  $C_{19}H_{27}NO_3$  317.42

D-Phenylalanine, *N*-[[*trans*-4-(1-methylethyl)cyclohexyl] carbonyl]-;

(-)-*N*-[(*trans*-4-Isopropylcyclohexyl)carbonyl]-D-phenylalanine CAS RN®: 105816-04-4; UNII: 41X3PWK402.

## DEFINITION

Nateglinide contains NLT 98.0% and NMT 102.0% of  $C_{19}H_{27}NO_3$ , calculated on the dried basis.

## IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **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

### PROCEDURE

**Buffer:** 8.5 g/L of anhydrous dibasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 7.5.

**Mobile phase:** Methanol and *Buffer* (1:1)

**System suitability stock solution:** 0.2 mg/mL each of [USP Nateglinide Related Compound C RS](#) and D,L-phenylalanine in methanol. [NOTE—Sonicate, if necessary.]

**System suitability solution:** Transfer [USP Nateglinide RS](#) to a suitable volumetric flask, dissolve first in methanol, using 45% of the final volume, add *System suitability stock solution* equal to 5% of the final volume, and then dilute with *Buffer* to volume to obtain a solution containing about 1.0 mg/mL of nateglinide and about 0.01 mg/mL each of nateglinide related compound C and D,L-phenylalanine.

**Standard solution:** 1.0 mg/mL of nateglinide prepared as follows: transfer [USP Nateglinide RS](#) to a suitable volumetric flask, dissolve first in methanol, using 50% of the final volume, and then dilute with *Buffer* to volume.

**Sample solution:** Transfer about 100 mg of Nateglinide to a 100-mL volumetric flask, dissolve in 50 mL of methanol, and dilute with *Buffer* to volume.

### Chromatographic system

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

**Mode:** LC

**Detector:** UV 210 nm

**Column:** 6-mm × 15-cm; 6-μm packing L71 (see [Chromatographic Reagents](#) under *Reagents, Indicators, and Solutions*)

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection size:** 20 μL

### System suitability

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

#### Suitability requirements

**Resolution:** NLT 0.9 between nateglinide related compound C and nateglinide, *System suitability solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

### Analysis

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

Calculate the percentage of nateglinide ( $C_{19}H_{27}NO_3$ ) in the portion of Nateglinide taken:

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

$r_U$  = peak response from the *Sample solution*

$r_S$  = peak response from the *Standard solution*

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

$C_U$  = concentration of Nateglinide in the *Sample solution* (mg/mL)

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

#### IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **LIMIT OF NATEGLINIDE RELATED COMPOUND A AND OTHER IMPURITIES**

**Buffer:** 7.8 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 2.5.

**Mobile phase:** Acetonitrile and *Buffer* (7:13)

**System suitability stock solution:** Dissolve [USP Nateglinide Related Compound A RS](#) in acetonitrile to obtain a solution containing about 0.6 mg/mL. Further dilute this solution with *Mobile phase* to obtain a solution containing about 0.12 mg/mL.

**System suitability solution:** Transfer an amount of [USP Nateglinide RS](#) to a suitable volumetric flask, dissolve first in acetonitrile using 10% of the final volume, then add *System suitability stock solution* equal to 10% of the final volume, and dilute with *Mobile phase* to volume to obtain a solution containing about 6 mg/mL of nateglinide and about 0.012 mg/mL of nateglinide related compound A.

**Standard solution:** Dissolve [USP Nateglinide RS](#) in acetonitrile to obtain a solution having a known concentration of about 0.3 mg/mL. Further dilute this solution with *Mobile phase* to obtain a solution having a known concentration of about 0.06 mg/mL.

**Sample solution:** Transfer 60 mg of Nateglinide to a 10-mL volumetric flask, dissolve in a minimal amount of acetonitrile, and dilute with *Mobile phase* to volume.

#### Chromatographic system

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

**Mode:** LC

**Detector:** UV 210 nm

**Column:** 3.9-mm × 5-cm; 5-μm packing L7

**Column temperature:** 40°

**Flow rate:** 2 mL/min

**Injection size:** 100 μL

**Run time:** 5 times the retention time of nateglinide

#### System suitability

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

#### Suitability requirements

**Resolution:** NLT 2.5 between nateglinide related compound A and nateglinide, *System suitability solution*

**Relative standard deviation:** NMT 2.0%, *Standard solution*

#### Analysis

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

Calculate the percentage of each impurity in the portion of Nateglinide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

$r_U$  = peak response of each impurity from the *Sample solution*

$r_S$  = peak response of nateglinide from the *Standard solution*

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

$C_U$  = concentration of Nateglinide in the *Sample solution* (mg/mL)

$F$  = relative response factor (see [Table 1](#))

#### Acceptance criteria

**Individual impurities:** See [Table 1](#).

**Table 1**

| Name                                        | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---------------------------------------------|-------------------------|--------------------------|------------------------------|
| Nateglinide related compound A <sup>a</sup> | 0.5                     | 0.015                    | 0.2                          |



**Documents**

Document Sharing Hub