

BRIEFING

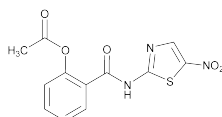
Nitazoxanide. This monograph has been posted on the USP Pending Monographs Web page for review and public comment for more than 90 days. No comments were received. The Small Molecules 1 Expert Committee has reviewed the draft and approved the monograph as an Authorized USP Pending Monograph. The liquid chromatographic procedures in the test for *Organic Impurities* and the *Assay* are based on analyses performed with the YMC-Pack C8 brand of L7 column. The typical retention times for the nitazoxanide peak are 5.7 min and 17 min for the *Assay* and the *Organic Impurities* test, respectively. A Description and Solubility section is added in this briefing.

Description and Solubility: White or yellowish, crystalline powder. Soluble in *N,N*-dimethylacetamide; very slightly soluble in alcohol; practically insoluble in water.

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Nitazoxanide

v.1 Authorized January 1, 2011



C₁₂H₉N₃O₅S 307.28
2-(Acetyloxy)-*N*-(5-nitro-2-thiazolyl) benzamide;
N-(5-Nitrothiazol-2-yl)salicylamide acetate ester [55981-09-4].

DEFINITION

Nitazoxanide contains NLT 98.0% and NMT 102.0% of C₁₂H₉N₃O₅S, calculated on the dried basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** (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**

Mobile phase: Acetonitrile and water (adjusted with phosphoric acid to a pH of 2.5) (3:2)

Standard solution: 0.1 mg/mL of USP Nitazoxanide RS in acetonitrile

Sample solution: 0.1 mg/mL of Nitazoxanide in acetonitrile

Chromatographic system

(See *Chromatography* (621), *System Suitability*.)

Mode: LC

Detector: UV 240 nm

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

Flow rate: 1 mL/min

Injection size: 20 μL

Run time: 2 times the retention time of nitazoxanide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of C₁₂H₉N₃O₅S in the portion of Nitazoxanide taken:

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

- r_u = peak response of nitazoxanide from the *Sample solution*
- r_s = peak response of nitazoxanide from the *Standard solution*
- C_s = concentration of USP Nitazoxanide RS in the *Standard solution* (mg/mL)
- C_u = concentration of Nitazoxanide in the *Sample solution* (mg/mL)

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

IMPURITIES

Inorganic Impurities:

- **RESIDUE ON IGNITION** (281): NMT 0.1%
- **HEAVY METALS, Method II** (231): NMT 10 ppm

Organic Impurities

• **PROCEDURE**

Solution A: Acetonitrile

Solution B: Water (adjusted with phosphoric acid to a pH of 2.5)

Diluent: *Solution A* and *Solution B* (7:3)

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	30	70
25.0	70	30
30.0	70	30
30.1	30	70
40.0	30	70

Standard solution: 2.5 μg/mL each of USP Nitazoxanide RS, USP Nitazoxanide Related Compound A RS, USP Aspirin RS, and USP Salicylic Acid RS in *Diluent*. [NOTE—Inject immediately.]

System suitability solution: Use the *Standard solution*. [NOTE—This solution can be analyzed for about 20 min.]

Sample solution: 2.5 mg/mL of Nitazoxanide in *Diluent*. [NOTE—Inject immediately.]

Chromatographic system

(See *Chromatography* (621), *System Suitability*.)

Mode: LC

Detector: UV 210 nm

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

Flow rate: 1 mL/min

Injection size: 35 μL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.0 between nitazoxanide related compound A and aspirin

Tailing factor: NMT 2.0 for the nitazoxanide peak

Relative standard deviation: NMT 10.0% for the nitazoxanide peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Nitazoxanide 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 nitazoxanide from the *Standard solution*
- C_s = concentration of USP Nitazoxanide RS in the *Standard solution* (mg/mL)
- C_u = concentration of Nitazoxanide in the *Sample solution* (mg/mL)
- F = relative response factor (see *Impurity Table 1*)

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Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Nitazoxanide related compound A ^a	0.35	0.46	0.1
Aspirin ^b	0.48	0.91	0.1
Salicylic acid ^c	0.61	3.7	0.1
Nitazoxanide	1.0	—	—
Any individual unspecified impurity	—	1.0	0.1

^a 5-Nitrothiazole-2-amine.

^b 2-Acetoxybenzoic acid.

^c 2-Hydroxybenzoic acid.

SPECIFIC TESTS

- **Loss on Drying (731):** Dry a sample at 60° for 3 h: it loses NMT 0.50% of its weight.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS (11)**
 - USP Nitazoxanide RS
 - USP Aspirin RS
 - 2-Acetoxybenzoic acid.
C₉H₈O₄ 180.16
 - USP Nitazoxanide Related Compound A RS
 - 5-Nitrothiazole-2-amine.
C₃H₃N₃O₂S 145.14
 - USP Salicylic Acid RS
 - 2-Hydroxybenzoic acid.
C₇H₆O₃ 138.12