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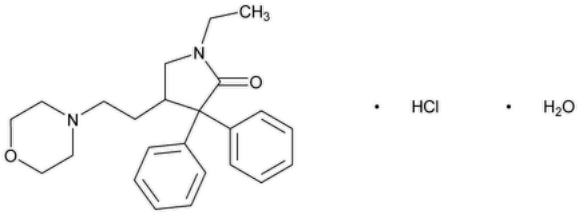
Doxapram Hydrochloride



$C_{24}H_{30}N_2O_2 \cdot HCl \cdot H_2O$ 432.99
$C_{24}H_{30}N_2O_2 \cdot HCl$ 414.97

2-Pyrrolidinone, 1-ethyl-4-[2-(4-morpholinyl)ethyl]-3,3-diphenyl-, monohydrochloride, monohydrate, (±)-;
(±)-1-Ethyl-4-(2-morpholinoethyl)-3,3-diphenyl-2-pyrrolidinone monohydrochloride monohydrate CAS RN®: 7081-53-0; UNII: P5RU6UOQ5Y.
Anhydrous CAS RN®: 113-07-5; UNII: FB8713U6DM.

DEFINITION

Doxapram Hydrochloride, dried at 105° for 2 h, contains NLT 98.0% and NMT 102.0% of doxapram hydrochloride ($C_{24}H_{30}N_2O_2 \cdot HCl$).

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** Identification Tests—General ⟨191⟩, *Chloride*: Meets the requirements

ASSAY

- **Procedure**

Solution A: To each L of water, add 0.1 mL of trifluoroacetic acid.

Solution B: To each L of acetonitrile, add 0.1 mL of trifluoroacetic acid.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20	50	50
25	50	50
25.1	90	10
30	90	10

Diluent: Acetonitrile and water (30:70)

Standard solution: 0.2 mg/mL of USP Doxapram Hydrochloride RS in *Diluent*

Sample solution: 0.2 mg/mL of Doxapram Hydrochloride in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 5-cm; 2.5-µm packing L1

Column temperature: 35°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

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 doxapram hydrochloride ($C_{24}H_{30}N_2O_2 \cdot HCl$) in the portion of Doxapram Hydrochloride taken:

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

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

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

C_S = concentration of USP Doxapram Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Doxapram Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0%, previously dried at 105° for 2 h

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.3%
- **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 2 mg/mL of USP Doxapram Hydrochloride RS and 0.04 mg/mL of USP Doxapram Related Compound B RS in *Diluent*

Standard solution: 0.004 mg/mL each of USP Doxapram Hydrochloride RS and USP Doxapram Related Compound B RS in *Diluent*

Sample solution: 2 mg/mL of Doxapram Hydrochloride in *Diluent*

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between doxapram related compound B and doxapram, *System suitability solution*

Relative standard deviation: NMT 5.0% for doxapram related compound B and doxapram, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of doxapram related compound B in the portion of Doxapram Hydrochloride taken:

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

r_U = peak response of doxapram related compound B from the *Sample solution*

r_S = peak response of doxapram related compound B from the *Standard solution*

C_S = concentration of USP Doxapram Related Compound B RS in the *Standard solution* (mg/mL)

C_U = concentration of Doxapram Hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of doxapram chloroethyl analog or any individual unspecified impurity in the portion of Doxapram Hydrochloride taken:

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

r_U = peak response of doxapram chloroethyl analog or any individual unspecified impurity from the *Sample solution*

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

C_S = concentration of USP Doxapram Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Doxapram Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Doxapram related compound B	0.9	0.2
Doxapram	1.0	—
Doxapram chloroethyl analog[a]	3.9	0.2
Any individual unspecified impurity	—	0.2
Total impurities	—	1.0

[a] 4-(2-Chloroethyl)-1-ethyl-3,3-diphenylpyrrolidin-2-one.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 10 mg/mL of Doxapram Hydrochloride in water

Acceptance criteria: 3.5–5.0

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: 3.0%–4.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨11⟩

USP Doxapram Hydrochloride RS

USP Doxapram Related Compound B RS

1-Ethyl-4-{2-[(2-hydroxyethyl)amino]ethyl}-3,3-diphenylpyrrolidin-2-one hydrochloride.

$C_{22}H_{29}ClN_2O_2$ 388.93

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
DOXAPRAM HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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