Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-FDD9F8D1-FAD8-4C66-AD8C-895AF30007B2_3_en-US
DOI: https://doi.org/10.31003/USPNF_M28080_03_01
DOI Ref: 09h00

Doxapram Hydrochloride Injection

DEFINITION

Doxapram Hydrochloride Injection is a sterile solution of Doxapram Hydrochloride in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of doxapram hydrochloride monohydrate ($C_{24}H_{30}N_2O_2 \cdot HCl \cdot H_2O$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

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: Nominally 0.2 mg/mL of doxapram hydrochloride monohydrate, equivalent to 0.19 mg/mL of doxapram hydrochloride from Injection in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. For *Identification* test *B*, use a diode array detector in the range of 190–300 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 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxapram hydrochloride monohydrate ($C_{24}H_{30}N_2O_2 \cdot HCl \cdot H_2O$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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 = nominal concentration of doxapram hydrochloride monohydrate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of doxapram hydrochloride monohydrate, 432.99

M_{r2} = molecular weight of anhydrous doxapram hydrochloride, 414.97

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **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 of USP Doxapram Hydrochloride RS in *Diluent*

Sample solution: Nominally 2 mg/mL of doxapram hydrochloride monohydrate, equivalent to 1.9 mg/mL of doxapram hydrochloride from Injection 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%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of doxapram related compound B, doxapram chloroethyl analog, or any individual unspecified degradation product in the portion of Injection taken:

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

r_U = peak response of each corresponding 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 = nominal concentration of doxapram hydrochloride monohydrate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Doxapram related compound B	0.9	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Doxapram	1.0	—
Doxapram chloroethyl analog[a]	3.9	0.2
Any individual unspecified degradation product	—	0.2
Total impurities	—	1.0

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

SPECIFIC TESTS

- **pH ⟨791⟩:** 3.5–5.0
- **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 3.3 USP Endotoxin Units/mg of doxapram hydrochloride.
- **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass. Store at controlled room temperature.
- **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 INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(4)

Current DocID: GUID-FDD9F8D1-FAD8-4C66-AD8C-895AF30007B2_3_en-US
Previous DocID: GUID-FDD9F8D1-FAD8-4C66-AD8C-895AF30007B2_1_en-US
DOI: https://doi.org/10.31003/USPNF_M28080_03_01
DOI ref: 09h00