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Doxylamine Succinate Tablets

DEFINITION

Doxylamine Succinate Tablets contain NLT 92.0% and NMT 108.0% of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$).

IDENTIFICATION

Delete the following:

▲• **A.** Tablets meet the requirements under *Identification—Organic Nitrogenous Bases ⟨181⟩*.▲ (USP 1-May-2019)

Add the following:

▲• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

Add the following:

▲• **B.** The UV-Vis absorption spectra of the major peak of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the corresponding peak of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 50 mM ammonium acetate in water; adjusted with glacial acetic acid to a pH of 4.0

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
2	90	10
15	40	60
20	40	60
21	90	10
25	90	10

Diluent: *Solution A* and *Solution B* (90:10)

Standard solution: 0.1 mg/mL of USP Doxylamine Succinate RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of doxylamine succinate in *Diluent* prepared as follows. Transfer an appropriate quantity of doxylamine succinate from NLT 10 finely powdered Tablets to a suitable volumetric flask and dilute with *Diluent* to volume. [Note—Sonication or shaking may be necessary. Centrifuge or pass a portion of this solution through a suitable filter.]

Chromatographic system

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

Mode: LC

Detector: UV 262 nm. For *Identification B*, use a diode array detector in the range of 230–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 µL

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 the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$) in the portion of Tablets taken:

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

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

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

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

C_U = nominal concentration of doxylamine succinate in the *Sample solution* (mg/mL)▲ (USP 1-May-2019)

Acceptance criteria: 92.0%–108.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)▲ (USP 1-May-2019)

Mode: UV

Analytical wavelength: 262 nm

Standard solution: USP Doxylamine Succinate RS in *Medium*

Sample solution: Sample per *Dissolution* ⟨711⟩. Dilute with *Medium* to a concentration that is similar to the *Standard solution*.

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$) dissolved.

Tolerances: NLT 80% (*Q*) of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$) is dissolved.

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

▲▲ (USP 1-May-2019)

IMPURITIES

Add the following:

▲• **Organic Impurities**

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

System suitability solution: 0.001 mg/mL each of USP Doxylamine Succinate RS and USP Carbinoxamine Related Compound C RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Doxylamine Succinate RS in *Diluent*

Sample solution: Nominally 1.0 mg/mL of doxylamine succinate in *Diluent* prepared as follows. Finely powder NLT 10 Tablets and transfer a portion of the powder to an appropriate volumetric flask. Dilute with *Diluent* to volume. [Note—Sonication or shaking may be necessary. Centrifuge or pass a portion of this solution through a suitable filter.]

System suitability

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

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

Suitability requirements

Resolution: NLT 2.0 between doxylamine and carbinoxamine related compound C, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified and unspecified degradation product in the portion of Tablets taken:

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

r_U = peak response of each specified and unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of doxylamine succinate in the *Sample solution* (mg/mL)

F = relative response factor of each specified and any unspecified degradation product (see *Table 2*)

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

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Doxylamine pyridinyl *N*-oxide[a]	0.64	2.1	0.2
Doxylamine dioxide[b]	0.70	1.8	0.2
Doxylamine pyridine-4-yl isomer[c,d]	0.81	—	—
Carbinoxamine related compound C[d]	0.95	—	—
Doxylamine	1.0	—	—
Doxylamine ethylamine *N*-oxide[e]	1.06	1.0	0.2
Doxylamine alcohol[f]	1.30	1.8	0.2
2-Benzoylpyridine[d,g]	1.44	—	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	2.0▲ (USP 1-May-2019)

[a] 2-[1-(2-(Dimethylamino)ethoxy)-1-phenylethyl]pyridine 1-oxide.

[b] *N*,*N*-Dimethyl-2-(1-(1-oxidopyridin-2-yl)-1-phenylethoxy)ethan-1-amine oxide.

[c] *N*,*N*-Dimethyl-2-[1-phenyl-1-(pyridin-4-yl)ethoxy]ethan-1-amine.

[d] Process related impurity. Do not include in calculation of total degradation products.

[e] *N*,*N*-Dimethyl-2-[1-phenyl-1-(pyridin-2-yl)ethoxy]ethan-1-amine oxide.

[f] 1-Phenyl-1-(pyridin-2-yl)ethan-1-ol.

[g] Phenyl(pyridin-2-yl)methanone.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** ▲Store at controlled room temperature in tight,▲ (USP 1-May-2019) light-resistant containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

▲ USP Carbinoxamine Related Compound C RS

N,*N*-Dimethyl-2-[phenyl(pyridin-2-yl)methoxy]ethan-1-amine;
Desmethyl doxylamine.

$C_{16}H_{20}N_2O$ 256.35▲ (USP 1-May-2019)

USP Doxylamine Succinate RS

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

Topic/Question	Contact	Expert Committee
DOXYLAMINE SUCCINATE TABLETS	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

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