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# Hydroxyzine Hydrochloride Oral Solution

**DEFINITION**

Hydroxyzine Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$).

**IDENTIFICATION**

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the hydroxyzine peak 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:** Trifluoroacetic acid and water (0.1:99.9)

**Solution B:** Trifluoroacetic acid and acetonitrile (0.05: 99.95)

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 90 | 10 |
| 4 | 90 | 10 |
| 12 | 60 | 40 |
| 16 | 60 | 40 |
| 21 | 20 | 80 |
| 25 | 20 | 80 |
| 26 | 90 | 10 |
| 30 | 90 | 10 |

**Diluent:** Acetonitrile and water (30:70)

**Standard solution:** 0.05 mg/mL of USP Hydroxyzine Hydrochloride RS in *Diluent*

**Sample stock solution:** Nominally 0.5 mg/mL of hydroxyzine hydrochloride from Oral Solution in *Diluent* prepared as follows. Transfer a portion of Oral Solution, equivalent to 25 mg of hydroxyzine hydrochloride, to a 50-mL volumetric flask. Dissolve and dilute with *Diluent* to volume.

**Sample solution:** Nominally 0.05 mg/mL of hydroxyzine hydrochloride from the *Sample stock solution* in *Diluent*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 230 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

**Column:** 2.1-mm × 15-cm; 1.8-µm packing L1

**Column temperature:** 30°

**Flow rate:** 0.3 mL/min

**Injection volume:** 2 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 hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) in the portion of Oral Solution taken:

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

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

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

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

$C_U$ = nominal concentration of hydroxyzine hydrochloride in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

## PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩**

**For single-unit containers**

**Acceptance criteria:** Meets the requirements

• **Deliverable Volume ⟨698⟩**

**For multiple-unit containers**

**Acceptance criteria:** Meets the requirements

## IMPURITIES

• **Organic Impurities**

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

**Standard stock solution:** 25.0 µg/mL each of USP Hydroxyzine Hydrochloride RS, USP Hydroxyzine Related Compound A RS, and USP 4-Chlorobenzophenone RS in *Diluent*

**Standard solution:** 1.0 µg/mL each of USP Hydroxyzine Hydrochloride RS, USP Hydroxyzine Related Compound A RS, and USP 4-Chlorobenzophenone RS from the *Standard stock solution* in *Diluent*

**Sample solution:** Nominally 500 µg/mL of hydroxyzine hydrochloride from Oral Solution in *Diluent* prepared as follows. Transfer a portion of Oral Solution, equivalent to 25 mg of hydroxyzine hydrochloride, to a 50-mL volumetric flask. Dissolve and dilute with *Diluent* to volume.

**Chromatographic system**

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

**Mode:** LC

**Detectors**

**Hydroxyzine related compound A and hydroxyzine hydrochloride:** UV 230 nm

**4-Chlorobenzophenone:** UV 254 nm

**Column:** 2.1-mm × 15-cm; 1.8-µm packing L1

**Column temperature:** 30°

**Flow rate:** 0.3 mL/min

**Injection volume:** 2 µL

**System suitability**

**Sample:** *Standard solution*

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

**Suitability requirements**

**Resolution:** NLT 5.0 between hydroxyzine related compound A and hydroxyzine

**Relative standard deviation:** NMT 3.0% for hydroxyzine related compound A, hydroxyzine, and 4-chlorobenzophenone

**Analysis**

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

**For impurities detected at UV 230 nm**

Calculate the percentage of any individual unspecified degradation product in the portion of Oral Solution taken:

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

$r_U$ = peak response of any individual unspecified degradation product from the *Sample solution*

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

$C_S$ = concentration of USP Hydroxyzine Hydrochloride RS in the *Standard solution* (µg/mL)

$C_U$ = nominal concentration of hydroxyzine hydrochloride in the *Sample solution* (µg/mL)

**For 4-chlorobenzophenone detected at UV 254 nm**

Calculate the percentage of 4-chlorobenzophenone in the portion of Oral Solution taken:

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

$r_U$ = peak response of 4-chlorobenzophenone from the *Sample solution*

$r_S$ = peak response of 4-chlorobenzophenone from the *Standard solution*

$C_S$ = concentration of USP 4-Chlorobenzophenone RS in the *Standard solution* (µg/mL)

$C_U$ = nominal concentration of hydroxyzine hydrochloride in the *Sample solution* (µg/mL)

**Acceptance criteria:** See *Table 2*. Disregard any peak below 0.03%.

**Table 2**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Hydroxyzine related compound A[a] | 0.94 | — |
| Hydroxyzine | 1.0 | — |
| 4-Chlorobenzophenone | 1.4 | 0.2 |
| Any individual unspecified degradation product | — | 0.2 |
| Total degradation products | — | 0.75 |

[a] This is a process impurity that is controlled in the drug substance. It is not to be reported or included in the total degradation products.

**ADDITIONAL REQUIREMENTS**

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP 4-Chlorobenzophenone RS

4-Chlorobenzophenone.

$C_{13}H_9ClO$ 216.66

USP Hydroxyzine Hydrochloride RS

USP Hydroxyzine Related Compound A RS

*p*-Chlorobenzhydrylpiperazine;

Also known as 1-[(4-Chlorophenyl)phenylmethyl]piperazine.

$C_{17}H_{19}ClN_2$ 286.80



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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| HYDROXYZINE HYDROCHLORIDE ORAL SOLUTION | Documentary Standards Support | SM42020 Small Molecules 4 |

**Chromatographic Database Information:** Chromatographic Database

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