Metaxalone Tablets

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Posting Date	28–Aug–2020
Official Date	01–Sep–2020
Expert Committee	Chemical Medicines Monographs 4
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 4 Expert Committee has revised the Metaxalone Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution test.

Labeling information has been incorporated to support the inclusion of *Dissolution Test 2*.

The Metaxalone Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Mary Koleck, Senior Scientific Liaison (301-230-7420 or mpk@usp.org).

Revision Bulletin
Official: September 1, 2020

Metaxalone Tablets

DEFINITION

Metaxalone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of metaxalone ($C_{12}H_{15}NO_3$).

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*.

ASSAY

• **Procedure**

Buffer: 0.68 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 4.5.

Mobile phase: Methanol and *Buffer* (50:50)

Standard stock solution: 0.5 mg/mL of USP Metaxalone RS prepared as follows. Transfer a suitable amount of USP Metaxalone RS to a suitable volumetric flask. Add 50% of the flask volume of methanol and sonicate to dissolve. Dilute with *Buffer* to volume.

Standard solution: 0.05 mg/mL of USP Metaxalone RS from *Standard stock solution* in *Mobile phase*

Sample stock solution: Nominally 1.0 mg/mL of metaxalone from NLT 20 Tablets prepared as follows. Transfer a portion of finely powdered Tablets equivalent to NLT 500 mg of metaxalone to a suitable volumetric flask. Add 50% of the flask volume of methanol and sonicate for 10 min with occasional swirling. Shake on a mechanical shaker for 15 min. Add 40% of the flask volume of *Buffer* and allow the solution to cool to room temperature. Dilute with *Buffer* to volume. Pass a portion of the solution through a PVDF filter of 0.45-µm pore size. Discard the first 5 mL. Use the filtrate.

Sample solution: Nominally 0.05 mg/mL of metaxalone from *Sample stock solution* and *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of metaxalone

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 the labeled amount of metaxalone ($C_{12}H_{15}NO_3$) in the portion of Tablets taken:

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

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

= peak response of metaxalone from the *Standard solution*

r_S

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 1-Sep-2020)

Medium: 0.5% sodium lauryl sulfate; 900 mL

Apparatus 2: 100 rpm

Time: 60 min

Buffer, Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*, except use 270 nm for analysis.

Standard solution: (*L*/900) mg/mL of USP Metaxalone RS, where *L* is the label claim of metaxalone, in mg/Tablet, prepared as follows. Transfer a suitable quantity of USP Metaxalone RS to a suitable volumetric flask. Add 4% of the flask volume of methanol, sonicate to dissolve, and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable PVDF membrane filter of 0.45-µm pore size. Discard the first 5 mL of the filtrate and use the remaining amount for analysis.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metaxalone ($C_{12}H_{15}NO_3$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of the *Medium*, 900 mL

L = label claim of metaxalone (mg/Tablet)

Tolerances: NLT 60% (*Q*) of the labeled amount of metaxalone ($C_{12}H_{15}NO_3$) is dissolved.

▲**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 5 g/L of sodium dodecyl sulfate in water, deaerated; 900 mL

Apparatus 2: 100 rpm

Time: 120 min

Standard solution: (*L*/900) mg/mL of USP Metaxalone RS, where *L* is the label claim of metaxalone in mg/Tablet, prepared as follows. Transfer a suitable quantity of USP Metaxalone RS to a suitable volumetric flask. Add 5% of the flask volume of methanol, sonicate to dissolve, and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 272 nm

Cell: 0.2 cm

Blank: *Medium*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metaxalone ($C_{12}H_{15}NO_3$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of metaxalone from the *Sample solution*

A_S = absorbance of metaxalone from the *Standard solution*

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

V = volume of the *Medium*, 900 mL

L = label claim of metaxalone (mg/Tablet)

Tolerances: NLT 70% (Q) of the labeled amount of metaxalone ($C_{12}H_{15}NO_3$) is dissolved. ▲ (RB 1-Sep-2020)

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements
- **Organic Impurities**

Buffer, Mobile phase, Standard solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Impurity stock solution: 0.2 mg/mL each of USP Metaxalone Related Compound B RS and USP Metaxalone Related Compound C RS in methanol. Sonicate to dissolve if necessary.

Peak identification solution: 1 mg/mL of USP Metaxalone RS and 0.02 mg/mL each of USP Metaxalone Related Compound B RS and USP Metaxalone Related Compound C RS prepared as follows. Transfer a suitable quantity of USP Metaxalone RS to a suitable volumetric flask. Add 50% of the flask volume of methanol and sonicate to dissolve. Transfer suitable volumes of *Impurity stock solution* to the flask. Dilute with *Buffer* to volume.

Sensitivity solution: 0.5 µg/mL of USP Metaxalone RS from *Standard solution* and *Mobile phase*

Sample solution: Nominally 1.0 mg/mL of metaxalone prepared from NLT 20 Tablets as follows. Transfer a portion of NLT 20 finely powdered Tablets equivalent to NLT 500 mg of metaxalone to a suitable volumetric flask. Add 50% of the flask volume of methanol and sonicate for 10 min with occasional swirling. Shake on a mechanical shaker for 15 min. Add 40% of the flask volume of *Buffer* and cool to room temperature. Dilute with *Buffer* to volume. Pass a portion of the solution through a PVDF filter of 0.45-µm pore size. Discard the first 5 mL.

System suitability

Samples: *Peak identification solution* and *Sensitivity solution*

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Tailing factor: NMT 2.0, *Sensitivity solution*

Relative standard deviation: NMT 10.0% for the metaxalone peak, *Sensitivity solution*

Signal-to-noise ratio: NLT 25 for the metaxalone peak, *Sensitivity solution*

Analysis

Samples: *Standard solution*, *Peak identification solution*, and *Sample solution*

Use the *Peak identification solution* to identify the peaks.

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

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

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

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Metaxalone related compound B	0.35	0.15
Metaxalone	1.0	—
Metaxalone related compound C[a]	3.6	—
N-Benzylmetaxalone[b]	6.9	—
Any individual unspecified degradation product	—	0.10
Total degradation products	—	0.5

[a] Process impurity, included for peak identification only; monitored in the drug substance.

[b] 3-Benzyl-5-[(3,5-dimethylphenoxy)methyl]oxazolidin-2-one.

ADDITIONAL REQUIREMENTS

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

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.▲ (RB 1-Sep-2020)

• **USP Reference Standards** ⟨11⟩

USP Metaxalone RS

USP Metaxalone Related Compound B RS

1-Amino-3-(3,5-dimethylphenoxy)propan-2-ol.

$C_{11}H_{17}NO_2$ 195.26

USP Metaxalone Related Compound C RS

Bis[2-hydroxy-3-(3,5-dimethylphenoxy)propyl]amine.

$C_{22}H_{31}NO_4$ 373.49

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Not Applicable

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