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Ethacrynic Acid Tablets

DEFINITION
Ethacrynic Acid Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$).

IDENTIFICATION

Delete the following:

▲• **A. Ultraviolet Absorption**▲ (USP 1-Dec-2024)

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-Dec-2024)

Change to read:

• **B.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2024)

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** 1% (v/v) triethylamine solution in water prepared as follows. Transfer a suitable aliquot of triethylamine to an appropriate volumetric flask containing 90% of the flask volume of water.▲ (USP 1-Dec-2024) Adjust with phosphoric acid to a pH of 6.8 ▲▲ (USP 1-Dec-2024) and dilute with water to volume.▲▲ (USP 1-Dec-2024)

Mobile phase: Acetonitrile and *Buffer* (40:60). ▲▲ (USP 1-Dec-2024)

Diluent: Acetonitrile and water (40:60)

Standard solution: 0.5 mg/mL of USP Ethacrynic Acid RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of ethacrynic acid in *Diluent* prepared as follows. Transfer a portion of the powder from NLT 20 finely powdered Tablets, equivalent to about 50 mg of ethacrynic acid, to a 100-mL volumetric flask, add about 80 mL of *Diluent*, and shake or sonicate as necessary. Dilute with *Diluent* to volume, and mix.

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

Mode: LC

Detector: UV 254 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Dec-2024)

Column: 3.9-mm × 30-cm; ▲10-µm▲ (USP 1-Dec-2024) packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2 times the retention time of ethacrynic acid▲ (USP 1-Dec-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-Dec-2024)

Tailing factor: NMT ▲2.0▲ (USP 1-Dec-2024)

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) in the portion of Tablets taken:

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

r_U = peak response of ethacrynic acid from the *Sample solution*

r_S = peak response of ethacrynic acid from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 M phosphate buffer, ▲pH 8.0 (dissolve 13.6 g of monobasic potassium phosphate in water, adjust with 92.2 mL of 1 N sodium hydroxide VS to a pH of 8.0, and dilute with water to 1000 mL);▲ (USP 1-Dec-2024) 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: A known concentration of USP Ethacrynic Acid RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute suitably with *Medium*.

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)▲ (USP 1-Dec-2024)

Mode: UV

Analytical wavelength: 277 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) is dissolved.

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

Medium: Citrate buffer, pH 3.0 (dissolve 17.2 g of citric acid and 5.3 g of sodium citrate dihydrate in 1 L of water, and adjust with ▲1 N sodium hydroxide VS▲ (USP 1-Dec-2024) or 1 M acetic acid TS to a pH of 3.0 ▲▲ (USP 1-Dec-2024)); 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

▲Determine the percentage of the labeled amount of ethacrynic acid by using either the *Chromatographic procedure* or the *Spectrophotometric procedure*.

Chromatographic procedure

Buffer:▲ (USP 1-Dec-2024) 1% (v/v) triethylamine solution in water prepared as follows. Transfer a suitable aliquot of triethylamine to an appropriate volumetric flask containing 90% of the flask volume of water. Adjust with phosphoric acid to a pH of 6.8. ▲▲ (USP 1-Dec-2024) Dilute with water to volume.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Standard stock solution: ▲0.3▲ (USP 1-Dec-2024) mg/mL of USP Ethacrynic Acid RS prepared as follows. Transfer a portion of USP Ethacrynic Acid RS to a suitable volumetric flask and add methanol to 10% of the flask volume. Dilute with *Medium* to volume.

Standard solution: ▲(L/900)▲ (USP 1-Dec-2024) mg/mL of USP Ethacrynic Acid RS from the *Standard stock solution* in *Medium*, ▲where L is the label claim in mg/Tablet▲ (USP 1-Dec-2024)

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 277 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2.4 times the retention time of ethacrynic acid

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 ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) dissolved:

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

r_U = peak response of ethacrynic acid from the *Sample solution*

r_S = peak response of ethacrynic acid from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

▲**Spectrophotometric procedure**

Diluent: Acetonitrile and water (40:60)

Standard stock solution: 0.5 mg/mL of USP Ethacrynic Acid RS prepared as follows. Transfer a portion of USP Ethacrynic Acid RS to a suitable volumetric flask, add *Diluent* to 40% of the flask volume, and sonicate if necessary. Dilute with *Medium* to volume.

Standard solution: (L/900) mg/mL of USP Ethacrynic Acid RS from the *Standard stock solution* in *Medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 10-µm pore size.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 277 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

▲ (USP 1-Dec-2024)

Tolerances: NLT 80% (Q) of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: Citrate buffer, pH 3.0 (dissolve 17.4 g of citric acid, anhydrous and 2.7 g of sodium citrate dihydrate in 800 mL of water, adjust with 5 N sodium hydroxide TS to a pH of 3.0, and dilute with water to 1000 mL); 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Diluent: Phosphate buffer, pH 8.0 prepared as follows. Dissolve 13.6 g of potassium phosphate, monobasic in 800 mL of water, add 92 mL of 1 N sodium hydroxide VS, and dilute with water to 1000 mL. Adjust with 1 N sodium hydroxide VS to a pH of 8.0.

Standard stock solution: 0.3 mg/mL of USP Ethacrynic Acid RS, prepared as follows. Transfer a portion of USP Ethacrynic Acid RS to a suitable volumetric flask, add *Diluent* to 60% of the flask volume, and sonicate to dissolve. Dilute with *Diluent* to volume.

Standard solution: (*L*/900) mg/mL of USP Ethacrynic Acid RS from the *Standard stock solution* in *Medium*, where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discard a few milliliters, and collect the filtrate.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 277 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of ethacrynic acid ($C_{13}H_{12}Cl_2O_4$) is dissolved.

Change to read:

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

▲▲ (USP 1-Dec-2024)

Add the following:

▲IMPURITIES

• **Organic Impurities**

Buffer: 1% (v/v) triethylamine solution in water. Adjust with phosphoric acid to a pH of 6.8.

Solution A: Acetonitrile and *Buffer* (30:70)

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
0.5	100	0
0.7	95	5
1.3	95	5
3	70	30
11	70	30
12	100	0
15	100	0

Diluent: Acetonitrile, methanol, and water (25:25:50)

Identification solution: 0.03 mg/mL of USP Ethacrynic Acid Related Compound C RS in *Diluent*. Sonicate if necessary.

Standard solution: 2 µg/mL of USP Ethacrynic Acid RS in *Diluent*

Sensitivity solution: 1 µg/mL of USP Ethacrynic Acid RS from the *Standard solution* in *Diluent*

Sample solution: Nominally 1 mg/mL of ethacrynic acid in *Diluent* prepared as follows. Transfer a portion equivalent to 25 mg of ethacrynic acid from finely powdered Tablets (NLT 20), to a suitable volumetric flask, add *Diluent* to 70% of the flask volume, and sonicate for about 20 min with intermittent shaking. Dilute with *Diluent* to volume. Pass the solution through a suitable filter of 0.22-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 2.1-mm × 10-cm; 1.7-µm packing L7

Column temperature: 27°

Flow rate: 0.4 mL/min

Injection volume: 3 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Identification solution*, *Standard solution*, and *Sample solution*

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

Calculate the percentage of each impurity 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 impurity from the *Sample solution*

r_S = peak response of ethacrynic acid from the *Standard solution*

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ethacrynic acid oxirane analog[a]	0.65	1.6	0.2
Ethacrynic acid related compound A[b]	0.77	1.4	0.2
Ethacrynic acid	1.0	—	—
Ethacrynic acid trichloro analog[c]	1.43	1.5	0.2
Ethacrynic acid related compound C[d]	2.43	0.73	3.5
Any unspecified degradation product	—	1.0	0.2
Total impurities	—	—	4.0

[a] [2,3-Dichloro-4-(2-ethyloxirane-2-carbonyl)phenoxy]acetic acid.

[b] (4-Butyryl-2,3-dichlorophenoxy)acetic acid.

[c] {2,3-Dichloro-4-[2-(chloromethyl)butanoyl]phenoxy}acetic acid.

[d] Ethacrynic acid pyrane dimer.

▲ (USP 1-Dec-2024)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed containers. ▲Store at controlled room temperature.▲ (USP 1-Dec-2024)

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Ethacrynic Acid RS

▲ USP Ethacrynic Acid Related Compound C RS

{4-[2-(4-(Carboxymethoxy)-2,3-dichlorobenzoyl)-2,5-diethyl-3,4-dihydro-2*H*-pyran-6-yl]-2,3-dichlorophenoxy}acetic acid.

$C_{26}H_{24}Cl_4O_8$ 606.27▲ (USP 1-Dec-2024)

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

Topic/Question	Contact	Expert Committee
ETHACRYNIC ACID TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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