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Diflunisal Tablets

DEFINITION

Diflunisal Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diflunisal ($C_{13}H_8F_2O_3$).

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*.

Delete the following:

▲• **B. Thin-Layer Chromatography**

Standard solution: 10 mg/mL of USP Diflunisal RS in methanol and water (80:20)

Sample solution: Nominally 10 mg/mL of diflunisal prepared as follows. Transfer a quantity of finely ground Tablets, equivalent to about 100 mg of diflunisal, to a 10-mL volumetric flask. Add 2 mL of water, and sonicate for 5 min. Dilute with methanol to volume, sonicate for an additional 5 min, and pass through a suitable filter.

Chromatographic system

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

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: *n*-Hexane, glacial acetic acid, and chloroform (17:3:2)

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatogram until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, air-dry, and examine under long-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*. ▲ (USP 1-May-2020)

Add the following:

▲• **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-May-2020)

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Methanol, acetonitrile, glacial acetic acid, and water (40:17:6:45)

Diluent: Acetonitrile and water (60:40)

Standard solution: 0.1 mg/mL of USP Diflunisal RS in *Diluent*. Sonicate to dissolve as needed.

Sample stock solution: Nominally 1 mg/mL of diflunisal prepared as follows. Finely powder Tablets (NLT 20). Transfer a quantity of the powder, equivalent to about 100 mg of diflunisal, to a 100-mL volumetric flask. Add 5 mL of water and sonicate for 5 min. Add 60 mL of acetonitrile, and sonicate with occasional shaking for 10 min. Dilute with water to volume. Pass through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Sample solution: Nominally 0.1 mg/mL of diflunisal in *Diluent* from *Sample stock solution*

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.

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of diflunisal▲ (USP 1-May-2020)

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 diflunisal ($C_{13}H_8F_2O_3$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Citric acid solution: Dissolve 7 g of anhydrous citric acid in 100 mL of water.

0.1 M tris buffer: Dissolve 121 g of tris(hydroxymethyl)aminomethane (THAM) in 9 L of water. Adjust with *Citric acid solution* to a pH of 7.45, at 25°. Dilute with water to 10.0 L, equilibrate to 37°, and adjust to a pH of 7.20, if necessary.

Medium: *0.1 M tris buffer*; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

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

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

Instrumental conditions

▲(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)▲ (USP 1-May-2020)

Mode: UV

Analytical wavelength: 306 nm

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diflunisal ($C_{13}H_8F_2O_3$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

▲ (USP 1-May-2020)

Tolerances: NLT 80% (Q) of the labeled amount of diflunisal ($C_{13}H_8F_2O_3$) is dissolved.

Change to read:

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

▲▲ (USP 1-May-2020)

IMPURITIES

Add the following:

▲• **Organic Impurities**

Mobile phase: Methanol, acetonitrile, glacial acetic acid, and water (36:15:6:50)

Diluent: Acetonitrile and water (60:40)

Sensitivity solution: 1 µg/mL of USP Diflunisal RS in *Diluent*. Sonicate to dissolve as needed.

Standard solution: 2 µg/mL of USP Diflunisal RS in *Diluent*. Sonicate to dissolve as needed.

Sample solution: Prepare as directed in the *Sample stock solution* in the *Assay*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any unspecified 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 any unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of diflunisal in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Difluorobiphenol[a,b]	0.69	—
Diflunisal	1.0	—
Diflunisal acetophenone analog[a,c]	1.1	—
Diflunisal acetate analog[a,d]	1.3	—
Difluorobiphenyl[a,e]	2.1	—
Any unspecified degradation product	—	0.10
Total degradation products	—	0.5

[a] Process impurity for identification only. It is not to be reported or included in the total degradation products.

[b] 2',4'-Difluorobiphenyl-4-ol.

[c] 1-(2',4'-Difluorobiphenyl-4-yl)ethan-1-one.

[d] 2',4'-Difluorobiphenyl-4-yl acetate.

[e] 2,4-Difluorobiphenyl.

▲ (USP 1-May-2020)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed containers. ▲ Store at controlled room temperature.▲ (USP 1-May-2020)

• **USP Reference Standards ⟨11⟩**

USP Diflunisal RS

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

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

Chromatographic Database Information: Chromatographic Database

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