Sulindac Tablets

DEFINITION

Sulindac Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of sulindac ($C_{20}H_{17}FO_3S$).

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*.
- **B.** The UV-Vis spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **PROCEDURE**

Solution A: 0.1% formic acid in water
Solution B: •0.1%• (IRA 1-Jul-2017) formic acid in acetonitrile
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	70	30
8.0	70	30
15.0	10	90
18.0	10	90
18.1	70	30
20.0	70	30

Diluent: Acetonitrile and water (50:50)
System suitability solution: 0.018 mg/mL each of USP Sulindac RS, USP Sulindac Related Compound A RS, USP Sulindac Related Compound B RS, and USP Sulindac Related Compound C RS in *Diluent*
Standard solution: 0.2 mg/mL of USP Sulindac RS in *Diluent*
Sample solution: Nominally 0.2 mg/mL of sulindac in *Diluent* prepared as follows. Dissolve •a quantity nominally equivalent to 20 mg• (IRA 1-Jul-2017) of sulindac from finely powdered Tablets in 70 mL of *Diluent* in a 100-mL volumetric flask. Shake by mechanical means for 60 min and dilute with *Diluent* to volume. Shake for another 5 min. Centrifuge the solution for 10 min and inject the supernatant.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 330 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.
Column: 2.1-mm × 15-cm; 1.7-µm packing L1
Column temperature: 45°
Flow rate: 0.3 mL/min
Injection volume: 2 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—See *Table 2* for the relative retention times.]
Suitability requirements
Resolution: NLT 4.0 between sulindac and sulindac related compound A; NLT 4.0 between sulindac related compound A and sulindac related compound B, *System suitability solution*
Tailing factor: NMT 2.0, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of sulindac ($C_{20}H_{17}FO_3S$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Sulindac RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of sulindac in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION** ⟨711⟩

Medium: 0.1 M pH 7.2 phosphate buffer prepared as directed in *Reagents, Indicators, and Solutions—Buffer Solutions*, except to use twice the stated quantities of the monobasic potassium phosphate solution and of the sodium hydroxide solution; 900 mL
Apparatus 2: 50 rpm
Time: 45 min
Standard solution: 20 µg/mL of USP Sulindac RS in *Medium*
Sample solution: Pass 20 mL of the solution under test through a suitable filter, transfer 10 mL of the filtrate to a 100-mL volumetric flask, and dilute with *Medium* to volume.
Blank: *Medium*
Instrumental conditions
Mode: UV
Analytical wavelength: Maximum absorbance at about 326 nm
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of sulindac ($C_{20}H_{17}FO_3S$) 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 Sulindac RS in the *Standard solution* (mg/mL)
D = dilution volume
V = volume of *Medium*, 900 mL
L = label claim (mg/Tablet)
Tolerances: NLT 80% (Q) of the labeled amount of sulindac ($C_{20}H_{17}FO_3S$) is dissolved.

Change to read:

- **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩: •Meet the requirements• (IRA 1-Jul-2017)

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 0.018 mg/mL each of USP Sulindac RS, USP Sulindac Related Compound A RS, USP Sulindac Related Compound B RS, and USP Sulindac Re-

lated Compound C RS in *Diluent*. Sonicate for 2–5 min and mix with inversion.

Sample solution: Nominally 0.6 mg/mL of sulindac in *Diluent* prepared as follows. Dissolve a quantity nominally equivalent to 60 mg of sulindac from finely powdered Tablets in 70 mL of *Diluent* in a 100-mL volumetric flask. Shake by mechanical means for 60 min and dilute with *Diluent* to volume. Shake for another 5 min. Centrifuge the solution for 10 min. Collect and inject the supernatant.

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 4.0 between sulindac and sulindac related compound A; NLT 4.0 between sulindac related compound A and sulindac related compound B

Relative standard deviation: •NMT 2.0% for sulindac, sulindac related compound B, and sulindac related compound C• (ERR 1-Aug-2016)

Analysis

Samples: *Standard solution* and *Sample solution*

•Calculate the percentage of sulindac related compound B or sulindac related compound C in the portion of Tablets taken:• (ERR 1-Aug-2016)

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

r_U = •peak response of sulindac related compound B or sulindac related compound C from the *Sample solution*• (ERR 1-Aug-2016)

r_S = •peak response of sulindac related compound B or sulindac related compound C from the *Standard solution*• (ERR 1-Aug-2016)

C_S = concentration of the corresponding related compound in the *Standard solution* (mg/mL)

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

Calculate the percentage of any individual unspecified impurity 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 individual unspecified impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sulindac	1.0	—
Sulindac related compound A	1.26	—[a]
Sulindac related compound B	1.36	0.5
Sulindac related compound C	1.70	0.5
Individual unspecified impurity	—	0.1
Total impurities	—	3.0

[a] Sulindac related compound A is controlled in the API. Therefore, no individual acceptance criteria is needed. Sulindac related compound B and sulindac related compound C are both degradants and process impurities.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Sulindac RS
  USP Sulindac Related Compound A RS
  (*E*)-2-{5-Fluoro-2-methyl-1-[4-(methylsulfinyl)benzylidene]-1*H*-inden-3-yl}acetic acid.
  $C_{20}H_{17}FO_3S$ 356.41
  USP Sulindac Related Compound B RS
  (*Z*)-2-{5-Fluoro-2-methyl-1-[4-(methylsulfonyl)benzylidene]-1*H*-inden-3-yl}acetic acid.
  $C_{20}H_{17}FO_4S$ 372.41
  USP Sulindac Related Compound C RS
  (*Z*)-2-{5-Fluoro-2-methyl-1-[4-(methylthio)benzylidene]-1*H*-inden-3-yl}acetic acid.
  $C_{20}H_{17}FO_2S$ 340.41