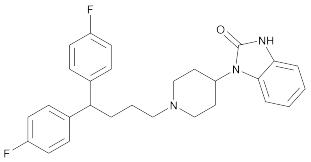
Pimozide



$C_{28}H_{29}F_2N_3O$ 461.55

2*H*-Benzimidazol-2-one, 1-[1-[4,4-bis(4-fluorophenyl)butyl]-4-piperidinyl]-1,3-dihydro-;
1-[1-[4,4-Bis(*p*-fluorophenyl)butyl]-4-piperidyl]-2-benzimidazolinone [2062-78-4].

DEFINITION

Pimozide contains NLT 98.0% and NMT 102.0% of pimozide ($C_{28}H_{29}F_2N_3O$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** •**INFRARED ABSORPTION** ⟨**197**⟩**:** [NOTE—Methods described in ⟨197K⟩ or ⟨197A⟩ may be used.]• (IRA 1-Nov-2016)
- **B.** The retention time 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: 2.5 g/L of ammonium acetate and 8.5 g/L of tetrabutylammonium hydrogen sulfate in water
Solution B: Acetonitrile
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
10	70	30
15	70	30
20	80	20
25	80	20

System suitability solution: 0.05 mg/mL of USP Pimozide RS and 0.02 mg/mL of USP Mebendazole RS in methanol
Standard solution: 1 mg/mL of USP Pimozide RS in methanol
Sample solution: 1 mg/mL of Pimozide in methanol. [NOTE—Sonication may be needed to dissolve the sample.]
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 10-cm; 3-µm packing L1
Flow rate: 2 mL/min
Injection volume: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—See *Table 2* for the relative retention times.]
Suitability requirements
Resolution: NLT 5.0 between pimozide and mebendazole, *System suitability solution*
Tailing factor: NMT 2.0, *Standard solution*
Relative standard deviation: NMT 0.73%, •• (IRA 1-Nov-2016) *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of pimozide ($C_{28}H_{29}F_2N_3O$) in the portion of Pimozide taken:

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

r_U = peak response of pimozide from the *Sample solution*
r_S = peak response of pimozide from the *Standard solution*
C_S = concentration of USP Pimozide RS in the *Standard solution* (mg/mL)
C_U = concentration of Pimozide in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.2%

Delete the following:

•• **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm• (Official 1-Jan-2018)

Change to read:

- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 0.05 mg/mL of USP Pimozide RS in methanol
Sample solution: 10 mg/mL of Pimozide in methanol. [NOTE—Sonication may be needed to dissolve the sample.]
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—See *Table 2* for the relative retention times.]
Suitability requirements
Resolution: NLT 5.0 between pimozide and mebendazole, *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 each impurity in the portion of Pimozide taken:

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

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of pimozide from the *Standard solution*
C_S = concentration of USP Pimozide RS in the *Standard solution* (mg/mL)
C_U = concentration of Pimozide in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Pimozide amine[a]	0.1	0.5
Mebendazole[b]	0.88	—
Desfluoro pimozide[c]	0.9	0.5
o-Pimozide isomer[d]	0.95	0.5
Pimozide	1.0	—
Didehydropimozide[e]	1.1	0.5
●Pimozide olefin[f]	1.2	0.5● (IRA 1-Nov-2016)
Pimozide *N*-oxide[g]	1.3	0.5
Any individual unspecified impurity	—	0.10
Total impurities	—	●1.0● (IRA 1-Nov-2016)

[a] 1-(Piperidin-4-yl)benzimidazolin-2-one.

[b] Included for system suitability purposes only. Not a process impurity or degradation product.

[c] 1-{1-[4-(4-Fluorophenyl)-4-phenylbutyl]piperidin-4-yl}benzimidazolin-2-one.

[d] ●1-{1-[4-(2-Fluorophenyl)-4-(4-fluorophenyl)butyl]piperidin-4-yl}-1*H*-benzimidazol-2-one.● (IRA 1-Nov-2016)

[e] 1-{1-[4,4-Bis(4-fluorophenyl)butyl]-1,2,3,6-tetrahydropyridin-4-yl}benzimidazolin-2-one.

[f] ●1-{1-[4,4-Bis(4-fluorophenyl)but-3-en-1-yl]piperidin-4-yl}benzimidazolin-2-one.● (IRA 1-Nov-2016)

[g] 1-[4,4-Bis(4-fluorophenyl)butyl]-4-(2-oxobenzimidazol-1-yl)piperidine 1-oxide.

SPECIFIC TESTS

- **Loss on Drying** ⟨731⟩
  Analysis: Dry at 105° to a constant weight.
  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.

- **USP Reference Standards** ⟨11⟩
  USP Mebendazole RS
  USP Pimozide RS