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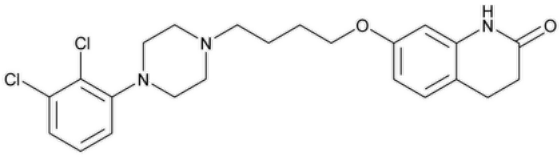
Aripiprazole



$C_{23}H_{27}Cl_2N_3O_2$ 448.39

2(1*H*)-Quinolinone, 7-[4-[4-(2,3-dichlorophenyl)-1- piperazinyl]butoxy]-3,4-dihydro-;

7-[4-[4-(2,3-Dichlorophenyl)-1-piperazinyl]butoxy]-3,4-dihydrocarbostyril CAS RN®: 129722-12-9; UNII: 82VFR53I78.

DEFINITION

Aripiprazole contains NLT 98.0% and NMT 102.0% of aripiprazole ($C_{23}H_{27}Cl_2N_3O_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **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

• **Procedure**

Protect the solutions from light.

Diluent: Acetonitrile, methanol, water, and acetic acid (30:10:60:1)

Solution A: Acetonitrile and 0.05% trifluoroacetic acid (10:90)

Solution B: Acetonitrile and 0.05% trifluoroacetic acid (90:10)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
2	80	20
10	65	35
20	10	90
25	10	90
26	80	20
35	80	20

[Note—The gradient was established on an HPLC system with a dwell volume of approximately 650 µL.]

System suitability solution: 1 µg/mL each of USP Aripiprazole RS and USP Aripiprazole Related Compound F RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Aripiprazole RS in *Diluent*

Sample solution: 0.1 mg/mL of Aripiprazole in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 10-cm; 3-µm packing L1

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for aripiprazole and aripiprazole related compound F are 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 2.0 between aripiprazole and aripiprazole related compound F, *System suitability solution*

Tailing factor: NMT 1.5 for aripiprazole, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of aripiprazole ($C_{23}H_{27}Cl_2N_3O_2$) in the portion of Aripiprazole taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

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

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

• **ORGANIC IMPURITIES**

Protect the solutions from light.

Diluent, Solution A, Solution B, Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Aripiprazole taken:

$$\text{Result} = (r_i/r_U) \times (1/F) \times 100$$

r_i = peak response of each impurity from the *Sample solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Aripiprazole related compound G[a]	0.9	0.72	0.10
Aripiprazole	1.0	—	—
Aripiprazole related compound F[b,c]	1.1	1.0	0.10
Aripiprazole 4,4'-dimer[d]	1.3	1.0	0.10
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	0.50

[a]

[a] 7-{4-[4-(2,3-Dichlorophenyl)piperazin-1-yl]butoxy}quinolin-2(1*H*)-one.

[b] 4-(2,3-Dichlorophenyl)-1-[4-(2-oxo-1,2,3,4-tetrahydroquinolin-7-yloxy)butyl]piperazine 1-oxide.

[c] If possible from the manufacturing process.

[d] 1,1'-(Ethane-1,1-diyl)bis(2,3-dichloro-4-{4-[3,4-dihydroquinolin-2(1*H*)-one-7-yloxybutyl]piperazin-1-yl}benzene).

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Aripiprazole RS

USP Aripiprazole Related Compound F RS

4-(2,3-Dichlorophenyl)-1-[4-(2-oxo-1,2,3,4-tetrahydroquinolin-7-yloxy)butyl]piperazine 1-oxide.
$C_{23}H_{27}Cl_2N_3O_3$ 464.38

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

Topic/Question	Contact	Expert Committee
ARIPIPRAZOLE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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