Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-28F6A917-A21C-4749-ACD0-6945D1F45859_2_en-US
DOI: https://doi.org/10.31003/USPNF_M2432_02_01
DOI Ref: q7tz4

Aripiprazole Orally Disintegrating Tablets

DEFINITION
Aripiprazole Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of aripiprazole ($C_{23}H_{27}Cl_2N_3O_2$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197A**▲ (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**

Solution A: 2.84 g/L of sodium sulfate in water

Buffer: 3.48 g/L of dibasic potassium phosphate adjusted with phosphoric acid to a pH of 8.2

Mobile phase: Acetonitrile and *Buffer* (50:50)

Diluent A: Acetonitrile, methanol, *Solution A*, and glacial acetic acid (33:11:56:1)

Diluent B: Acetonitrile and 0.1 M hydrochloric acid (20:80)

System suitability solution: 0.01 mg/mL each of USP Aripiprazole RS and USP Aripiprazole Related Compound G RS in *Diluent A*. Sonication and shaking may be used to aid in dissolution.

Standard solution: 0.25 mg/mL of USP Aripiprazole RS in *Diluent B*. Sonication may be used to aid in dissolution.

Sample solution: Nominally 0.2–0.3 mg/mL of aripiprazole from NLT 5 Orally Disintegrating Tablets prepared as follows. Transfer NLT 5 Orally Disintegrating Tablets to a suitable volumetric flask and dilute with *Diluent B* to NMT 75% of the final flask volume. Sonicate for 5 min and shake for 15 min. Dilute with *Diluent B* to volume. Pass the resulting solution through a suitable filter and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 252 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.4 times the retention time of aripiprazole

System suitability

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

[Note—The relative retention times of aripiprazole related compound G and aripiprazole are 0.74 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between aripiprazole related compound G and aripiprazole, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of aripiprazole ($C_{23}H_{27}Cl_2N_3O_2$) in the portion of Orally Disintegrating 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 Aripiprazole RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩:** NMT 60 s

• **Dissolution ⟨711⟩**

Medium: pH 4.0 sodium acetate trihydrate buffer (3.0 g/L of sodium acetate prepared as follows. Transfer a suitable quantity of sodium acetate to a suitable container containing 90% of the final container volume of water. Adjust with glacial acetic acid to a pH of 4.0. Add water to the final volume.), degassed; 1000 mL

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Acetonitrile and 0.025 M hydrochloric acid (40:60)

Standard solution: (*L*/1000) mg/mL of USP Aripiprazole RS in *Mobile phase* where *L* is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter, discarding the first few mL.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of aripiprazole

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of aripiprazole ($C_{23}H_{27}Cl_2N_3O_2$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of aripiprazole ($C_{23}H_{27}Cl_2N_3O_2$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Solution A: Water and trifluoroacetic acid (100:0.05)

Solution B: Acetonitrile and trifluoroacetic acid (100:0.05)

Solution C: 2.84 g/L of sodium sulfate in water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20	70	30
40	42	58
50	10	90
55	10	90

Time (min)	Solution A (%)	Solution B (%)
56	90	10
60	90	10

[NOTE—The gradient was established on an HPLC system with a dwell volume of approximately 1.0 mL.]

Diluent: Acetonitrile, methanol, *Solution C*, and glacial acetic acid (33:11:56:1)

System suitability solution: 250 µg/mL of USP Aripiprazole RS, and 0.5 µg/mL each of USP Aripiprazole Related Compound F RS and USP Aripiprazole Related Compound G RS in *Diluent*. Sonication may be used to aid in dissolution.

Sample solution: Nominally 0.2–0.3 mg/mL of aripiprazole from NLT 5 Orally Disintegrating Tablets prepared as follows. Transfer NLT 5 Orally Disintegrating Tablets to a suitable volumetric flask. Add about 70% of the total volume of *Diluent*. Sonicate for 10 min and shake for 10 min. Dilute with *Diluent* to volume. Pass the resulting solution through a suitable filter and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

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

Suitability requirements

Resolution: NLT 4.0 between aripiprazole related compound G and aripiprazole; NLT 1.5 between aripiprazole and aripiprazole related compound F

Analysis

Sample: *Sample solution*

Calculate the total peak response for individual impurities and aripiprazole from the *Sample solution*:

$$\text{Result} = \Sigma[r_i \times (1/F)] + r_U$$

r_i = peak response of each degradation product from the *Sample solution*

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

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

Calculate the percentage of each degradation product in the portion of Orally Disintegrating Tablets taken:

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

r_i = peak response of each degradation product from the *Sample solution*

r_T = total peak response for individual impurities and aripiprazole from the *Sample solution*

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

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Aripiprazole related compound G	0.96	0.77	0.3
Aripiprazole	1.0	—	—
Aripiprazole related compound F	1.03	1.0	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Any individual unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.0

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

USP Aripiprazole Related Compound G RS

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

$C_{23}H_{25}Cl_2N_3O_2$ 446.37

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(1)

Current DocID: GUID-28F6A917-A21C-4749-ACD0-6945D1F45859_2_en-US

DOI: https://doi.org/10.31003/USPNF_M2432_02_01

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