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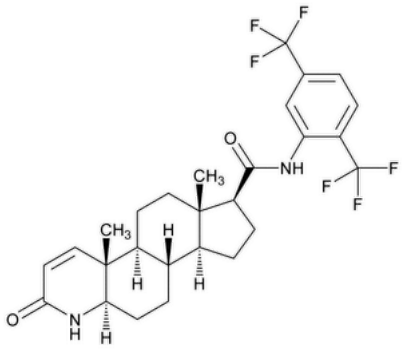
Dutasteride

Change to read:



$C_{27}H_{30}F_6N_2O_2$ ▲528.54▲ (CN 1-Aug-2024)

(5α,17β)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-azaandrost-1-ene-17-carboxamide;

α,α,α,α',α',α'-Hexafluoro-3-oxo-4-aza-5α-androst-1-ene-17β-carboxy-2',5'-xylidide CAS RN®: 164656-23-9.

DEFINITION

Dutasteride contains NLT 97.0% and NMT 102.0% of dutasteride ($C_{27}H_{30}F_6N_2O_2$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A, 197K, or 197M

• **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**

Diluent: Acetonitrile and water (60:40)

Mobile phase: Acetonitrile, water, and trifluoroacetic acid (52: 48: 0.025)

System suitability solution: 0.5 mg/mL of USP Dutasteride Resolution Mixture RS in *Diluent*. Sonicate to dissolve.

Standard solution: 0.5 mg/mL of USP Dutasteride RS in *Diluent*. Sonicate to dissolve.

Sample solution: 0.5 mg/mL of Dutasteride in *Diluent*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of dutasteride

System suitability

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

[Note—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between dutasteride 17α-epimer and dutasteride, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dutasteride ($C_{27}H_{30}F_6N_2O_2$) in the portion of Dutasteride taken:

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

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

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

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

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

Acceptance criteria: 97.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Limit of Residual Solvents**

Standard stock solution: 5 mg/mL each of acetonitrile, ethyl acetate, pyridine, toluene, dioxane, and *n*-heptane in dimethyl sulfoxide

Standard solution: 10 µg/mL each of acetonitrile, ethyl acetate, pyridine, toluene, dioxane, and *n*-heptane in dimethyl sulfoxide from the *Standard stock solution*

Sample solution: 10 mg/mL of Dutasteride in dimethyl sulfoxide

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m; capillary coated with 5-µm film of phase G1

Temperatures

Injection port: 180°

Detector: 260°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	—	50	3
50	10	200	2

Carrier gas: Helium

Flow rate: Head pressure at 12 psi

Split flow: 10 mL/min

Septum purge: 2 mL/min

Injector type: Headspace

Sample volume: 2 mL

Temperatures

Sample: 85°

Needle: 100°

Transfer line: 110°

Times

Equilibration: 1 min

Thermostating: 15 min

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.2 between *n*-heptane and dioxane peaks

Relative standard deviation: NMT 5% for each solvent

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each solvent in the portion of Dutasteride taken:

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

r_U = peak response of each solvent from the *Sample solution*

r_S = peak response of each solvent from the *Standard solution*

C_S = concentration of each solvent in the *Standard solution* (mg/mL)

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Acetonitrile	0.30	0.3
Ethyl acetate	0.60	0.2
Dioxane	0.83	0.1
n-Heptane	0.85	0.5
Pyridine	0.92	0.2
Toluene	1.0	0.2

• **Organic Impurities, Procedure 1**

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

System suitability

Sample: *System suitability solution*

[Note—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between dutasteride 17α-epimer and dutasteride

Analysis

Sample: *Sample solution*

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

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

r_U = peak area for each impurity from the *Sample solution*

r_T = sum of all the peak areas from the *Sample solution*

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Dutasteride acid[a]	0.10	1.0	0.2
Dutasteride dimethylamide[b]	0.11	1.4	0.2
Dutasteride methyl ester[c]	0.28	1.0	0.15
Dutasteride ethyl ester[d]	0.39	1.0	0.2
Dutasteride 17α-5-ene[e]	0.90	1.0	0.2
Dutasteride 17α-epimer	0.93	1.0	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Dutasteride	1.00	—	—
Chlorodutasteride[f]	1.15	0.33	0.4
Dutasteride 5-ene[g]	1.20	1.0	0.3
Any unspecified impurity	—	—	0.1

[a] (5α,17β)-3-Oxo-4-azaandrost-1-ene-17-carboxylic acid.

[b] (5α,17β)-*N*,*N*-Dimethyl-3-oxo-4-azaandrost-1-ene-17-carboxamide.

[c] Methyl (5α,17β)-3-oxo-4-azaandrost-1-ene-17-carboxylate.

[d] Ethyl (5α,17β)-3-oxo-4-azaandrost-1-ene-17-carboxylate.

[e] (17α)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-azaandrost-1,5(6)-diene-17-carboxamide.

[f] (1α,5α,17β)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-1-chloro-3-oxo-4-azaandrostane-17-carboxamide.

[g] (17β)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-azaandrost-1,5(6)-diene-17-carboxamide.

Change to read:

• **Organic Impurities, Procedure 2**

Diluent, System suitability solution, and **Sample solution:** Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile and water (80:20)

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 5-µm packing L11

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 5 times the retention time of dutasteride

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between dutasteride α-dimer and dutasteride β-dimer peaks

Analysis

Sample: *Sample solution*

Integrate the dutasteride peak and all drug-related peaks eluting after the dutasteride peak.

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

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

r_U = peak area of each impurity from the *Sample solution*

r_T = sum of all the peak areas from the *Sample solution*

F = relative response factor (see *Table 4*)

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Dutasteride	1.0	—	—
Dihydrodutasteride[a]	1.19	1.0	0.15
Dutasteride α-dimer	3.7	1.0	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Dutasteride β-dimer	4.3	1.0	0.5
Any unspecified impurity	—	1.0	0.1
Total impurities[b]	—	—	2.0

[a] ▲*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-aza-5α-androstane-17β-carboxamide.▲ (CN 1-Aug-2024)

[b] Sum of impurities from *Table 3* and *Table 4*.

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I, Method Ic*

Sample: 100 mg

Analysis: The *Sample* is heated in a tube at 180° for 4 min in a stream of dry inert gas.

Acceptance criteria

For the anhydrous form: NMT 0.50%

For the hydrate form: NMT 2.0%. *Water Determination* ⟨921⟩, *Method I, Method Ia* may also be used.

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL in chloroform and alcohol (98:2)

Acceptance criteria: +15.0° to +25.0°

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store below 30°.

• **Labeling:** Where it is the hydrate form, the label so indicates.

• **USP Reference Standards** ⟨11⟩

USP Dutasteride RS

USP Dutasteride Resolution Mixture RS

The mixture contains Dutasteride and the following three impurities (other impurities may also be present):

Dutasteride 17α-epimer: (5α,17α)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-azaandrost-1-ene-17-carboxamide.

$C_{27}H_{30}F_6N_2O_2$ 528.53

Dutasteride α-dimer: {[(5α,17β)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-azaandrost-1-ene-17-carboxamide-]4-yl}{[(5α,17α)-3-oxo-4-azaandrost-1-ene]-17-yl}methanone.

$C_{46}H_{55}F_6N_3O_4$ 827.94

Dutasteride β-dimer: {[(5α,17β)-*N*-[2,5-Bis(trifluoromethyl)phenyl]-3-oxo-4-azaandrost-1-ene-17-carboxamide-]4-yl}{[(5α,17β)-3-oxo-4-azaandrost-1-ene]-17-yl}methanone.

$C_{46}H_{55}F_6N_3O_4$ 827.94

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

Topic/Question	Contact	Expert Committee
DUTASTERIDE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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