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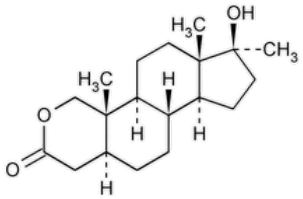
Oxandrolone



$C_{19}H_{30}O_3$ 306.44

2-Oxaandrostan-3-one, 17-hydroxy-17-methyl-, (5α,17β)-.

17β-Hydroxy-17-methyl-2-oxa-5α-androstan-3-one CAS RN®: 53-39-4; UNII: 7H6TM3CT4L.

» Oxandrolone contains not less than 98.0 percent and not more than 102.0 percent of $C_{19}H_{30}O_3$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩—

USP Oxandrolone RS

USP Oxandrolone Related Compound A RS
(7,8-Didehydro-oxandrolone) or (17β-hydroxy-17α-methyl-2-oxa-5α-androst-7-en-3-one).

USP Oxandrolone Related Compound B RS
(4-Oxa-isomer) or (17β-hydroxy-17α-methyl-4-oxa-5α-androstan-3-one).

USP Oxandrolone Related Compound C RS
Anhydro-oxandrolone or (17,17-dimethyl-18-nor-2-oxa-5α-androst-13-en-3-one).

Identification—

Change to read:

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

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Specific rotation ⟨781S⟩**:** between −18° and −24°.

Test solution: 10 mg per mL, in chloroform.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.2%.

Related compounds—

Solution A: acetonitrile.

Solution B: water.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Blank solution—Prepare a mixture of *Solution A* and *Solution B* (50:50).

Standard stock solution—Dissolve accurately weighed quantities of USP Oxandrolone Related Compound A RS, USP Oxandrolone Related Compound B RS, USP Oxandrolone Related Compound C RS, and USP Oxandrolone RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, with acetonitrile to obtain a solution having known concentrations of about 4 µg of USP Oxandrolone Related Compound A RS per mL, 120 µg of USP Oxandrolone Related Compound B RS per mL, 4 µg of USP Oxandrolone Related Compound C RS per mL, and 200 µg of USP Oxandrolone RS per mL. [Note—Sonicate if necessary to dissolve.]

Standard solution—Dilute 1.0 mL of the *Standard stock solution* with 4.0 mL of acetonitrile and 5.0 mL of water, and mix.

Test solution—Weigh accurately 40 mg of Oxandrolone into a 10-mL volumetric flask, dissolve in 5.0 mL of acetonitrile using an ultrasonic bath, dilute with water to volume, and mix.

[Note—The *Test solution,* the *Standard solution,* and the *Blank solution* are made up fresh and injected immediately.]

Chromatographic system—The liquid chromatograph is equipped with a 210-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The column temperature is maintained at 40°. The flow rate is about 0.7 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	50	50	equilibration
0–30	50→100	50→0	linear gradient
30–32	100→50	0→50	linear gradient
32–40	50	50	re-equilibration

Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between oxandrolone related compound A and oxandrolone related compound B is not less than 1.5, and the resolution, *R,* between oxandrolone related compound B and oxandrolone is not less than 2.0; the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections is not more than 5.0%.

Change to read:

Procedure—Separately inject equal volumes (about 50 µL) of the *Blank solution,* the *Standard solution,* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of oxandrolone related compound A in the portion of Oxandrolone taken by the formula:

$$(C/W)(r_U/r_S)$$

in which *C* is the concentration, in µg per mL, of oxandrolone related compound A in the *Standard solution; W* is the weight, in mg, of Oxandrolone taken to prepare the *Test solution;* r_U is the peak area of oxandrolone related compound A in the chromatogram of the *Test solution;* and r_S is the peak area obtained for oxandrolone related compound A in the chromatogram of the *Standard solution*.

Calculate the percentage of oxandrolone related compound C, methyltestosterone, Δ1-mestalone, specified unknown impurity 1, and each impurity eluting at a relative retention time greater than or equal to 2.2 (relative to retention time of oxandrolone) by the formula:

$$(1/F)(C/W)(r_U/r_S)$$

in which *F* is the relative response factor (see accompanying table for values); *C* is the concentration, in µg per mL, of oxandrolone related compound C in the *Standard solution; W* is the weight, in mg, of Oxandrolone taken to prepare the *Test solution;* r_U is the peak area of oxandrolone related compound C, methyltestosterone, Δ1-mestalone, specified unknown impurity 1, or each impurity eluting at a relative retention time greater than or equal to 2.2 in the chromatogram of the *Test solution;* and r_S is the peak area obtained for oxandrolone related compound C in the chromatogram of the *Standard solution*.

Calculate the percentage of each impurity, except oxandrolone related compound A, oxandrolone related compound C, methyltestosterone, Δ1-mestalone, specified unknown impurity 1, and other impurities eluting at relative retention times greater than or equal to 2.2 by the formula:

$$(1/F)(C/W)(r_U/r_S)$$

in which *F* is the relative response factor for each impurity (see accompanying table for values); *C* is the concentration, in µg per mL, of USP Oxandrolone RS in the *Standard solution; W* is the weight, in mg, of Oxandrolone taken to prepare the *Test solution;* r_U is the peak area of each impurity, in the chromatogram of the *Test solution,* other than peak areas of oxandrolone related compound A, oxandrolone related compound C, methyltestosterone, Δ1-mestalone, specified unknown impurity 1, and other impurities eluting at relative retention times greater than or equal to 2.2; and r_S is the peak area obtained for oxandrolone in *Standard solution.* Disregard any peak observed in the chromatogram obtained from the *Blank solution*. Disregard any impurity peak that is less than 0.05%. The impurities meet the requirements specified in the accompanying table.

Compound	Relative Retention Time	Relative Response Factor (*F*)	Limit (%)
Secodicarboxylic acid[1]	0.46	4.1	0.1

Compound	Relative Retention Time	Relative Response Factor (*F*)	Limit (%)
7,8-Didehydro-oxandrolone[2] (Oxandrolone related compound A)	0.90	—	0.1
4-Oxa-isomer[3] (Oxandrolone related compound B)	0.94	1.4	0.3
Oxandrolone	1.00	—	—
Oxandrolone open lactone methyl ester[4]	1.09	1.5	0.1
Secoacid anhydride[5]	1.12	2.5	0.1
Methyltestosterone[6]	1.25	0.8[a]	0.1
17-epi-Oxandrolone[7]	1.33	1.0	0.3
Δ1-Mestalone[8]	1.48	1.3[a]	0.1
4-Oxa-isomer (beta epimer)[9]	1.52	1.4	0.3
Specified unknown impurity 1	1.63	0.6[a]	0.1
Oxandrolone-17-acetate[10]	2.14	1.9	0.1
Anhydro-oxandrolone[11] (Oxandrolone related compound C)	3.29	—	0.5
Individual unknown impurity	—	1.0	0.1
Total impurities	—	—	1.0

[a] *F* values relative to oxandrolone related compound C.

[1] 17β-Hydroxy-17α-methyl-2-nor-5α-androstan-1,3-dioic acid.

[2] 17β-Hydroxy-17α-methyl-2-oxa-5α-androst-7-en-3-one.

[3] 17β-Hydroxy-17α-methyl-4-oxa-5α-androstan-3-one.

▲[4] Methyl 1,17β-dihydroxy-17α-methyl-1,3-seco-2-nor-5α-androstan-3-oate.▲ (ERR 1-Mar-2019)

[5] 17β-Hydroxy-17α-methyl-2-oxa-5α-androstan-1,3-dione.

[6] 17β-Hydroxy-17α-methyl-5α-androst-4-ene-3-one.

[7] 17α-Hydroxy-17β-methyl-2-oxa-5α-androstan-3-one.

[8] 17β-Hydroxy-17α-methyl-5α-androst-1-ene-3-one.

[9] 17β-Hydroxy-17α-methyl-4-oxa-5β-androstan-3-one.

[10] 17β-Hydroxy-17α-methyl-2-oxa-5α-androstan-3-one 17-acetate.

[11] 17,17-Dimethyl-18-nor-2-oxa-5α-androst-13-en-3-one.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water and acetonitrile (50:50). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Oxandrolone RS in acetonitrile, and dilute quantitatively, and stepwise if necessary, with acetonitrile to obtain a solution having a known concentration of about 3 mg per mL. [NOTE—Sonicate if necessary to dissolve.]

Assay preparation—Transfer to a suitable volumetric flask an accurately weighed quantity of Oxandrolone, and dissolve in and dilute with acetonitrile to volume to obtain a solution having a concentration of about 3 mg per mL.

Chromatographic system (see *CHROMATOGRAPHY* ⟨621⟩)—The liquid chromatograph is equipped with a 210-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 0.8 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency is not less than 2000 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{19}H_{30}O_3$ in the portion of Oxandrolone taken by the formula:

$$VC(r_U/r_S)$$

in which V is the final volume, in mL, of the *Assay preparation; C* is the concentration, in mg per mL, of USP Oxandrolone RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
OXANDROLONE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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