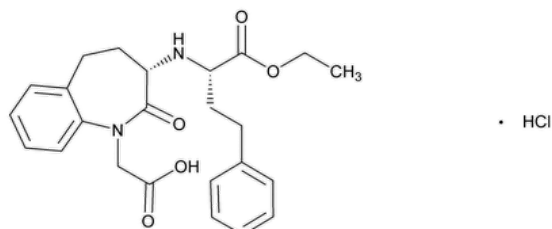


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Benazepril Hydrochloride



$C_{24}H_{28}N_2O_5 \cdot HCl$ 460.95

1*H*-1-Benzazepine-1-acetic acid, 3-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, monohydrochloride, [S-(*R*^{*},*R*^{*})].
 (3*S*)-3-[[1-(1*S*)-1-Carboxy-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-benzazepine-1-acetic acid, 3-ethyl ester, monohydrochloride CAS
 RN[®]: 86541-74-4; UNII: N1SN99T69T.

» Benazepril Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{24}H_{28}N_2O_5 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers, and store at a temperature below 30°, preferably between 15° and 30°.

Change to read:

USP REFERENCE STANDARDS (11).—

[USP Benazepril Hydrochloride RS](#)

[USP Benazepril Related Compound A RS](#)

▲2-[(*R*)-3-[(*R*)-1-Ethoxy-1-oxo-4-phenylbutan-2-yl]amino]-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl]acetic acid hydrochloride;

Also known as ▲ (ERR 1-Jul-2021) (3*R*) 3-[[1-(1*R*)-1-(Ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-benzazepine-1-acetic acid, monohydrochloride.

$C_{24}H_{28}N_2O_5 \cdot HCl$ 460.95

[USP Benazepril Related Compound B RS](#)

▲2-[(*S*)-3-[(*R*)-1-Ethoxy-1-oxo-4-phenylbutan-2-yl]amino]-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl]acetic acid hydrochloride;

Also known as ▲ (ERR 1-Jul-2021) (3*S*) 3-[[1-(1*R*)-1-(Ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-benzazepine-1-acetic acid, monohydrochloride.

$C_{24}H_{28}N_2O_5 \cdot HCl$ 460.95

[USP Benazepril Related Compound C RS](#)

▲(S)-2-[(*S*)-1-(Carboxymethyl)-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-3-yl]amino]-4-phenylbutanoic acid;

Also known as ▲ (ERR 1-Jul-2021) 3-(1-Carboxy-3-phenyl-1(*S*)-propyl)amino-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3*S*)-benzazepine-1-acetic acid.

$C_{22}H_{24}N_2O_5$ 396.44

[USP Benazepril Related Compound D RS](#)

▲2-[(*S*)-3-[(*S*)-4-Cyclohexyl-1-ethoxy-1-oxobutan-2-yl]amino]-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl]acetic acid hydrochloride;

Also known as ▲ (ERR 1-Jul-2021) (3-(1-Ethoxycarbonyl-3-cyclohexyl-1(*S*)-propyl)amino)-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3*S*)-benzazepine)-1-acetic acid, monohydrochloride.

$C_{24}H_{34}N_2O_5 \cdot HCl$ 467.00

[USP Benazepril Related Compound E RS](#)

▲(S)-2-(3-Amino-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)acetic acid hydrochloride;

Also known as ▲ (ERR 1-Jul-2021) 3-Amino-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3*S*)-benzazepine-1-acetic acid ▲monohydrochloride.

$C_{12}H_{14}N_2O_3 \cdot HCl$ 270.71▲ (ERR 1-Jul-2021)

[USP Benazepril Related Compound F RS](#)

▲*tert*-Butyl (S)-2-(3-amino-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)acetate;

Also known as ▲ (ERR 1-Jul-2021) *tert*-Butyl-3-amino-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3*S*)-benzazepine-1-acetic acid.

▲ $C_{16}H_{22}N_2O_3$ 290.36▲ (ERR 1-Jul-2021)

[USP Benazepril Related Compound G RS](#)

▲Ethyl (S)-2-[(*S*)-1-(2-ethoxy-2-oxoethyl)-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-3-yl]amino]-4-phenylbutanoate;

Also known as ▲ (ERR 1-Jul-2021) (3-(1-Ethoxycarbonyl-3-phenyl-1(*S*)-propyl)amino)-2,3,4,5-tetrahydro-2-oxo-1*H*-1-(3*S*)-benzazepine)-1-acetic acid ethyl ester.

▲ $C_{26}H_{32}N_2O_5$ 452.55▲ (ERR 1-Jul-2021)

Identification—

A: [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197M](#).

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*.

C: It responds to the test for [Chloride \(191\)](#).

Absorbance of solution—The absorbance of a 1 in 100 solution of it in methanol, determined in a 1-cm cell at 420 nm, is not more than 0.015, methanol being used as the blank.

Absorptivity—

*Test preparation—*Dissolve an accurately weighed quantity of Benazepril Hydrochloride in methanol, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.025 mg per mL.

*Procedure—*Proceed as directed under [Ultraviolet-Visible Spectroscopy \(857\)](#), and measure the absorbance at 238 nm: the absorptivity is between 21.0 and 23.2.

LOSS ON DRYING (731)—Dry it at 105° for 3 hours: it loses not more than 1.5% of its weight.

RESIDUE ON IGNITION (281)—Ignite at 600°. Not more than 0.1% residue is found.

Related compounds—

TEST 1 (FOR BENAZEPRIL RELATED COMPOUND A)—

*pH 6.0 Phosphate buffer—*Dissolve 9.66 g of monobasic potassium phosphate and 2.68 g of dibasic sodium phosphate, heptahydrate in about 900 mL of water, and dilute with water to 1000 mL.

*Mobile phase—*Prepare a filtered and degassed mixture of *pH 6.0 Phosphate buffer* and methanol (80:20). Make adjustments if necessary (see *System Suitability* under [Chromatography \(621\)](#)).

*Resolution solution—*Dissolve accurately weighed quantities of [USP Benazepril Hydrochloride RS](#) and [USP Benazepril Related Compound A RS](#) in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having known concentrations of about 1.0 mg per mL and 0.005 mg per mL, respectively.

*Standard stock solution—*Dissolve an accurately weighed quantity of [USP Benazepril Related Compound A RS](#) in *Mobile phase* to obtain a solution having a known concentration of about 0.05 mg per mL.

*Standard solution—*Dilute a suitable portion of *Standard stock solution*, accurately measured, with *Mobile phase* to obtain a solution having a known concentration of about 5 µg per mL.

*Dilute standard solution—*Dilute a suitable portion of *Standard stock solution*, accurately measured, with *Mobile phase* to obtain a solution having a known concentration of about 1 µg per mL.

*Test solution—*Transfer about 50 mg of Benazepril Hydrochloride, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see [CHROMATOGRAPHY \(621\)](#))—The liquid chromatograph is equipped with a 240-nm detector and a 4.0-mm × 10-cm column that contains packing L41. The flow rate is about 0.9 mL per minute. The column temperature is maintained at 30°. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure*: the resolution, *R*, between benazepril hydrochloride and benazepril related compound A is not less than 2.0. Chromatograph the *Dilute standard solution*, and record the peak responses as directed for *Procedure*: the signal-to-noise ratio is not less than 10:1. Chromatograph the *Standard solution*: the relative standard deviation for replicate injections determined from the benazepril related compound A peak is not more than 10%.

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

$$100(C_s/C_T)(r_U/r_S)$$

in which C_s is the concentration, in mg per mL, of [USP Benazepril Related Compound A RS](#) in the *Standard solution*; C_T is the concentration, in mg per mL, of Benazepril Hydrochloride in the *Test solution*; r_U is the peak response for benazepril related compound A obtained from the *Test solution*; and r_S is the peak response for benazepril related compound A obtained from the *Standard solution*: The limit of benazepril related compound A is given in the table below.

Benazepril Related Compound	Relative Retention Time	Limit (%)
A ¹	2.3	0.1

¹ ((3R)-3-[[[(1R)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid, monohydrochloride

TEST 2 (FOR BENAZEPRIL RELATED COMPOUNDS B, C, D, E, F, AND G)—

Tetrabutylammonium bromide solution, *Mobile phase*, *System suitability solution*, and *Chromatographic system*— Proceed as directed in the *Assay*.