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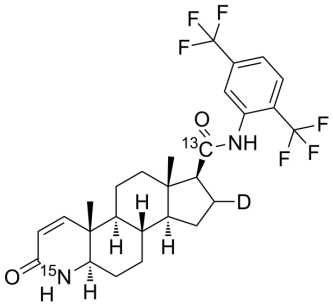
Dutasteride-^{13}C,^{15}N,d

Cat. No.:	HY-13613S2
Molecular Formula:	$C_{26}{}^{13}CH_{29}DF_6N^{15}NO_2$
Molecular Weight:	531.52
Target:	5 alpha Reductase; Apoptosis; Isotope-Labeled Compounds
Pathway:	Metabolic Enzyme/Protease; Apoptosis; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Dutasteride-^{13}C,^{15}N,d is ^{15}N and deuterated labeled Dutasteride (HY-13613). Dutasteride (GG745) is a potent inhibitor of both 5α-reductase isozymes. Dutasteride may possess off-target effects on the androgen receptor (AR) due to its structural similarity to DHT[1].
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Dutasteride inhibits ^{3}H-T conversion to ^{3}H-DHT and, as anticipated, inhibits T-induced secretion of PSA and proliferation. However the drug also inhibited DHT-induced PSA secretion and cell proliferation (IC_{50} approximately 1 μM)[2]. Dutasteride competes for binding the LNCaP cell AR with an IC_{50} approximately 1.5 μM. High concentrations of dutasteride (10-50 μM), but not finasteride, in steroid-free medium, resulted in enhanced cell death, possibly by apoptosis[2]. Dutasteride reduces cell viability and cell proliferation in both cell lines tested (androgen-responsive (LNCaP) and androgen-unresponsive (DU145) human prostate cancer (PCa)) [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GG745 has a terminal half-life of approximately 240 hr, and single doses of >10 mg decreased DHT levels significantly more than did single 5-mg doses of finasteride[4]. In placebo treated men without prostate cancer there was an 8.3% median increase in PSA at month 24 compared with -59.5% in those who received dutasteride, using doubled values to correct for dutasteride treatment[5]. Toxicity: Dutasteride may affect male fertility and steroid hormone dynamics. Therefore, a 21-day reproduction study was conducted to determine the effects of dutasteride (10, 32 and 100 μg/L) on fish reproduction. Exposure to dutasteride significantly reduced fecundity of fish and affected several aspects of reproductive endocrine functions in both males and females[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Lazier CB, et al. Dutasteride, the dual 5alpha-reductase inhibitor, inhibits androgen action and promotes cell death in the LNCaP prostate cancer cell line. Prostate. 2004 Feb 1;58(2):130-44.

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[3]. Bramson HN, et al. Unique preclinical characteristics of GG745, a potent dual inhibitor of 5AR. J Pharmacol Exp Ther. 1997 Sep;282(3):1496-502.

[4]. Andriole GL, et al. Clinical usefulness of serum prostate specific antigen for the detection of prostate cancer is preserved in men receiving the dual 5alpha-reductase inhibitor dutasteride. J Urol. 2006 May;175(5):1657-62.

[5]. Margiotta-Casaluci L, et al. Mode of action of human pharmaceuticals in fish: the effects of the 5-alpha-reductase inhibitor, dutasteride, on reproduction as a case study. Aquat Toxicol. 2013 Mar 15;128-129:113-23.

[6]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-216.

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