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产品名称：Enzalutamide
产品别名：恩杂鲁胺；MDV3100

生物活性：

Description	Enzalutamide (MDV3100) is an androgen receptor (AR) antagonist with an IC50 of 36 nM in LNCaP prostate cells.
IC_{50} & Target	IC50: 36 nM (androgen-receptor, in LNCaP cells)[1]
In Vitro	Enzalutamide has greater affinity to AR than Bicalutamide does in a competition assay with 16β-[^{18}F]fluoro-5α-DHT (18-FDHT) in castration-resistant LNCaP/AR cells (AR-overexpressing). While Enzalutamide shows no agonism in LNCaP/AR prostate cells. Enzalutamide antagonizes induction of prostate-specific antigen (PSA) and transmembrane serine protease 2 (TMPRSS2), combination with the synthetic androgen R1881 in parental LNCaP cells. Enzalutamide inhibits the transcriptional activity of a mutant AR protein (W741C, mutation of Trp741 to Cys)[1]. Enzalutamide also prevents nuclear translocation and co-activator recruitment of the ligand-receptor complex[2].
In Vivo	Enzalutamide induces great tumor regression in castrate male mice bearing LNCaP/AR xenografts at a dose of 10 mg/kg[1]. Enzalutamide shows dose-independent pharmacokinetics at intravenous and oral doses of 0.5-5 mg/kg[4].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 50 mg/mL (107.66 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1531 mL	10.7657 mL	21.5313 mL
5 mM	0.4306 mL	2.1531 mL	4.3063 mL
10 mM	0.2153 mL	1.0766 mL	2.1531 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.38 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

	2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.38 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Tran C, et al. Development of a second-generation antiandrogen for treatment of advanced prostate cancer. Science, 2009, 324 (5928), 787-790. [2]. Scher HI, et al. Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study. Lancet, 2010, 375(9724), 1437-1446. [3]. Guerrero J, et al. Enzalutamide, an androgen receptor signaling inhibitor, induces tumor regression in a mouse model of castration-resistant prostate cancer. Prostate. 2013 Sep;73(12):1291-305. [4]. Kim TH, et al. Pharmacokinetics of enzalutamide, an anti-prostate cancer drug, in rats. Arch Pharm Res. 2015 Nov;38(11):2076-82.

实验参考：

Cell Assay	LNCaP cells (10^7 cells/condition) are grown in RPMI media supplemented with 5% charcoalstripped serum for 22 days, then treated with DMSO or 1 nM R1881, combined with an antiandrogen (DMSO, 1 μM Bicalutamide, 10 μM Bicalutamide, 1 μM RD162, 10 μM RD162, 1 μM MDV3100, or 10 μM MDV3100) for 8 hours. An aliquot of cells are harvested for qRT-PCR of PSA and TMPRSS2 mRNA. The remaining cells are cross-linked using 1% paraformaldehyde for 10 minutes, then glycine is added and samples centrifuged (4°C, 4000 rpm, 5 minutes) to stop further crosslinking. Chromatin immunoprecipitation is performed using a chromatin immunoprecipitation assay kit. Immunoprecipitated DNA is amplified by real-time PCR. Primers are PSA enhancer forward-ATGTTCACATTAGTACACCTTGCC and reverse-TCTCAGATCCAGGCTTGCTTACTGTC and TMPRSS2 enhancer forward-TGGTCCTGGATGATAAAAAAAGTTT and reverse-GACATACGCCCCACAACAGA[1].
Animal Administration	Mice[3] Following a 5-day acclimation period, 5- to 9-week-old male CB17SCID mice are castrated and allowed to recover for an additional 5 days before inoculation with tumor cells. LNCaP cells co-expressing exogenous AR and the AR-dependent reporter construct ARR2-Pb-Luc (LNCaP-AR-Lux cells) are used to generate a xenograft model of human prostate cancer. Before implantation, LNCaP-AR-Lux cells are prepared by the addition of trypsin-EDTA, washed with complete medium, collected and resuspended at 20×10^6 cells/mL. Cell suspensions are diluted with Matrigel to 2×10^6 cells/0.2 mL and delivered subcutaneously in the suprascapular region. Tumor growth is monitored to the volume of 100 mm^3 when treatment begins (80 days). The observed rate of tumor take with LNCaP-AR-Lux cells is between 70% and 80%. Body weight and tumor volumes ($width^2\times length/2$) are measured two to three times per week with a digital caliper, and the average tumor volumes are determined. Test drugs are diluted in Tween 80:PEG 400, and stored at 4°C until administration by oral gavage. Each group of mice (n=7) is treated daily for 28 consecutive days with 1, 10, or 50 mg/kg Enzalutamide, vehicle control, or 50 mg/kg Bicalutamide. At the end of the

	treatment period or when tumor volume exceeded 1,000 mm^3, animals are euthanized and blood and tissue samples are collected for analysis. Rats[4] Male SD rats (n=3) are administered Enzalutamide through the tail vein (intravenous) and by oral gavage at 1 mg/kg and are kept in metabolic cages after dosing. Urine and feces samples are collected over the following time intervals after dosing: 0-2, 2-4, 4-6, 6-10, 10-24, 24-48, and 48-72 h. The metabolic cages are rinsed with distilled water, and residues are added to the urine samples at 72 h. To extract the Enzalutamide present in the feces, samples are shaken vigorously for 12 h with 50 % methanol.
References	[1]. Tran C, et al. Development of a second-generation antiandrogen for treatment of advanced prostate cancer. Science, 2009, 324 (5928), 787-790. [2]. Scher HI, et al. Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study. Lancet, 2010, 375(9724), 1437-1446. [3]. Guerrero J, et al. Enzalutamide, an androgen receptor signaling inhibitor, induces tumor regression in a mouse model of castration-resistant prostate cancer. Prostate. 2013 Sep;73(12):1291-305. [4]. Kim TH, et al. Pharmacokinetics of enzalutamide, an anti-prostate cancer drug, in rats. Arch Pharm Res. 2015 Nov;38(11):2076-82.