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产品名称：地加瑞克
产品别名：Degarelix

生物活性：

Description	Degarelix is a competitive and reversible gonadotropin-releasing hormone receptor (GnRHR) antagonist.
IC_{50} & Target	GnRHR[1]
In Vitro	Degarelix acts directly on the pituitary receptors for luteinizing hormone-releasing hormone (LHRH), blocking the action of endogenous LHRH. The use of degarelix eliminates the initial undesirable surge in gonadotropin and testosterone levels, which is produced by agonists of LHRH[1]. Degarelix treatment reduces cell viability in all prostate cell lines (WPE1-NA22, WPMY-1, BPH-1 cells, VCaP cells), with the exception of the PC-3 cells. The GnRH antagonist degarelix exerts a direct effect on prostate cell growth through apoptosis[2].
In Vivo	At single subcutaneous injections of 0.3 to 10 μg/kg in rats, degarelix produces a dose-dependent suppression of the pituitary-gonadal axis as revealed by the decrease in plasma luteinizing hormone (LH) and testosterone levels. Duration of LH suppression increases with the dose: in the rat, significant suppression of LH lasted 1, 2, and 7 days after a single subcutaneous injection of degarelix at 12.5, 50, or 200 μg/kg, respectively[3]. Degarelix is stable when incubated in microsomes and cryopreserved hepatocytes from animal liver tissue. In rat and dog, most of the degarelix dose is eliminated within 48 h via urine and feces in equal amounts (40–50% in each matrix), whereas in monkey the major route of excretion is fecal (50%) and renal (22%)[4].
Solvent&Solubility	***In Vitro:*** **H_2O : 25 mg/mL** (**15.32 mM**; Need ultrasonic) **DMSO : 10 mg/mL** (**6.13 mM**; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.6126 mL	3.0632 mL	6.1265 mL
	5 mM	0.1225 mL	0.6126 mL	1.2253 mL
	10 mM	0.0613 mL	0.3063 mL	0.6126 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: ≥ 1 mg/mL (0.61 mM); Clear solution

此方案可获得 ≥ 1 mg/mL (0.61 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 10.0 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% (20% SBE-β-CD in saline) Solubility: ≥ 1 mg/mL (0.61 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (0.61 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 1 mg/mL (0.61 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (0.61 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 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Rick FG, et al. An update on the use of degarelix in the treatment of advanced hormone-dependent prostate cancer. Onco Targets Ther. 2013 Apr 16;6:391-402. [2]. Sakai M, et al. In search of the molecular mechanisms mediating the inhibitory effect of the GnRH antagonistdegarelix on human prostate cell growth. PLoS One. 2015 Mar 26;10(3):e0120670. [3]. Broqua P, et al. Pharmacological profile of a new, potent, and long-acting gonadotropin-releasing hormoneantagonist: degarelix. J Pharmacol Exp Ther. 2002 Apr;301(1):95-102. [4]. Sonesson A, et al. Metabolite profiles of degarelix, a new gonadotropin-releasing hormone receptor antagonist, in rat, dog, and monkey. Drug Metab Dispos. 2011 Oct;39(10):1895-903.

实验参考：

Cell Assay	Cells are allowed to attach for 24–48 hours (h). After that, they are treated with different concentrations of degarelix, a GnRH antagonist (0.1 to 10 μM). 10 μL of MTT labeling reagent is added to each well and the plates are incubated at 37°C for 4h. Then, 100 μL of solubilization solution is added, and the plates are incubated at 37°C, overnight, in a humidified atmosphere. The final reaction is measured at 550–600 nm. The obtained absorbance directly correlates to the number of live and metabolically active cells, providing an indication of cell viability[2].
Animal Administration	Rats: To study the absorption, distribution, metabolism, and excretion, male and female rats are dosed with 30 μg [^{3}H]degarelix free base peptide/kg (-300 μCi/kg). Feces, heparin plasma, and urine samples from groups A and B are collected up to 240 h after dosing. Bile sampling from cannulated rats (group C) as well as urine and feces are collected for up to 48 h. All samples in this study are analyzed by LC-RAD at the contract research[4]. Monkeys: Four male cynomolgus Monkeys (4.2-7.5 kg) are dosed for a disposition of radioactivity study. The animals are administered a single subcutaneous dose of 8.2 μg/kg (200 μCi/kg) [^{3}H]degarelix. Urine and feces samples are collected quantitatively from each animal after dosing until the time of sacrifice. Blood samples are collected at the time of the sacrifice of the individual animal (6, 24, 48, and 240 h) into tubes containing EDTA as an anticoagulant[4].
	[1]. Rick FG, et al. An update on the use of degarelix in the treatment of advanced

References	hormone-dependent prostate cancer. Onco Targets Ther. 2013 Apr 16;6:391-402. [2]. Sakai M, et al. In search of the molecular mechanisms mediating the inhibitory effect of the GnRH antagonistdegarelix on human prostate cell growth. PLoS One. 2015 Mar 26;10(3):e0120670. [3]. Broqua P, et al. Pharmacological profile of a new, potent, and long-acting gonadotropin-releasing hormoneantagonist: degarelix. J Pharmacol Exp Ther. 2002 Apr;301(1):95-102. [4]. Sonesson A, et al. Metabolite profiles of degarelix, a new gonadotropin-releasing hormone receptor antagonist, in rat, dog, and monkey. Drug Metab Dispos. 2011 Oct;39(10):1895-903.