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产品名称：Gepotidacin
产品别名：GSK2140944

生物活性：

Description	Gepotidacin (GSK2140944) is a novel triazaacenaphthylene bacterial type II topoisomerase inhibitor.
In Vitro	Gepotidacin is a novel, first-in-class, triazaacenaphthylene antibacterial that inhibits bacterial DNA gyrase and topoisomerase IV via a unique mechanism and has demonstrated in vitro activity against gram-negative and gram-positive bacterias , including drug-resistant strains, and also targets pathogens associated with other conventional and biothreat infections. The MIC50 and MIC90 for gepotidacin against the 25 N. gonorrhoeae isolates tested are 0.12 and 0.25 μg/mL, respectively[1]. The gepotidacin MIC90s are as follows (in μg/mL): Streptococcus pyogenes, 0.25; Escherichia coli, 2; Moraxella catarrhalis, ≤ 0.06; Streptococcus pneumoniae, 0.25; Haemophilus influenzae, 1; Clostridium perfringens, 0.5; and Shigella spp., 1[2]. Gepotidacin hasin vitroactivity against causative pathogens of acute bacterial skin and skin structure infections (ABSSSIs)[3].
In Vivo	GSK2140944 MICs are 0.125 to 0.5 mg/L against the six MRSA isolates. ELF penetration ratios range from 1.1 to 1.4. Observed maximal decreases are 1.1 to 3.1 log10 CFU in neutropenic mice. The mean fAUC/MIC ratios required for stasis and 1-log-unit decreases are 59.3 ± 34.6 and 148.4 ± 83.3, respectively.

Solvent&Solubility

In Vitro:

DMSO： 7.14 mg/mL (15.92 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2296 mL	11.1478 mL	22.2956 mL
	5 mM	0.4459 mL	2.2296 mL	4.4591 mL
	10 mM	0.2230 mL	1.1148 mL	2.2296 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: ≥ 0.71 mg/mL (1.58 mM); Clear solution

此方案可获得 ≥ 0.71 mg/mL (1.58 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 7.1 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: ≥ 0.71 mg/mL (1.58 mM); Clear solution 此方案可获得 ≥ 0.71 mg/mL (1.58 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 7.1 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: ≥ 0.71 mg/mL (1.58 mM); Clear solution 此方案可获得 ≥ 0.71 mg/mL (1.58 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 7.1 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Farrell DJ, et al. In Vitro Activity of Gepotidacin (GSK2140944) against Neisseria gonorrhoeae. Antimicrob Agents Chemother. 2017 Feb 23;61(3). [2]. Biedenbach DJ, et al. In Vitro Activity of Gepotidacin, a Novel Triazaacenaphthylene Bacterial Topoisomerase Inhibitor, against a Broad Spectrum of Bacterial Pathogens. Antimicrob Agents Chemother. 2016 Jan 4;60(3):1918-23. [3]. O'Riordan W, et al. Efficacy, Safety, and Tolerability of Gepotidacin (GSK2140944) in the Treatment of Patients with Suspected or Confirmed Gram-Positive Acute Bacterial Skin and Skin Structure Infections. Antimicrob Agents Chemother. 2017 May 24;61(6). [4]. So W, et al. Pharmacodynamic Profile of GSK2140944 against Methicillin-Resistant Staphylococcus aureus in a Murine Lung Infection Model. Antimicrob Agents Chemother. 2015 Aug;59(8):4956-61.

实验参考：

Animal Administration	Mice: For neutropenic pharmacokinetic studies, at 3 h postinoculation (0 h), groups of 48 infected mice are administered GSK2140944 s.c. in single doses of 6.25, 50, or 200 mg/kg. Blood samples are collected from groups of six mice at 5 min and 0.25, 0.5, 1, 1.5, 2, 3, and 4 h postdose for 6.25- or 50-mg/kg doses and 5 min and 0.25, 0.5, 1, 1.5, 2, 4, and 6 h postdose for the 200-mg/kg dose via cardiac puncture[4].
References	[1]. Farrell DJ, et al. In Vitro Activity of Gepotidacin (GSK2140944) against Neisseria gonorrhoeae. Antimicrob Agents Chemother. 2017 Feb 23;61(3). [2]. Biedenbach DJ, et al. In Vitro Activity of Gepotidacin, a Novel Triazaacenaphthylene Bacterial Topoisomerase Inhibitor, against a Broad Spectrum of Bacterial Pathogens. Antimicrob Agents Chemother. 2016 Jan 4;60(3):1918-23. [3]. O'Riordan W, et al. Efficacy, Safety, and Tolerability of Gepotidacin (GSK2140944) in the Treatment of Patients with Suspected or Confirmed Gram-Positive Acute Bacterial Skin and Skin Structure Infections. Antimicrob Agents Chemother. 2017 May 24;61(6). [4]. So W, et al. Pharmacodynamic Profile of GSK2140944 against Methicillin-Resistant Staphylococcus aureus in a Murine Lung Infection Model. Antimicrob Agents Chemother. 2015 Aug;59(8):4956-61.