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产品名称: **Betrixaban**
产品别名: 贝曲西班 ; **PRT054021**

生物活性:						
Description		Betrixaban is a highly potent, selective, and orally efficacious factor Xa (fXa) inhibitor with IC50 of 1.5 nM.				
IC50 & Target		IC50: 1.5 nM (fXa)[1] Ki: 0.117 nM (fXa), 1.8 μM (hERG)[1]				
In Vitro		In patch clamp hERG assays, Betrixaban has IC50 of 8.9 μM. The plasma kallikrein IC50 and Ki values for Betrixaban are 6.3 μM and 3.5 μM respectively. Betrixaban (hERG Ki 1.8 μM) exhibits significantly lower hERG activity than all the others (hERG Ki≤0.5 μM)[1].				
In Vivo		Dosed at 0.5 mg/kg IV and 2.5 mg/kg PO, Betrixaban has bioavailability of 51.6% in dog; dosed at 0.75 mg/kg IV and 7.5 mg/kg PO, Betrixaban has bioavailability of 58.7% in monkey[1]. Both Betrixaban and Apixa-ban-mediated whole-blood INR increases are similarly reversed by r-Antidote. After i.v. infusion of the three fXa inhibitors (each administered individually) for 30 min, the total plasma concentrations of rivaroxaban, Betrixaban and apixaban are 1.4±0.4 μM (mean±s.d.), 0.2±0.01 μM and 1.4±0.3 μM, respectively, and the percentages of unbound inhibitor are 2.2%±0.8% (mean±s.d.), 40%±7.2% and 1.5%±0.3%, respectively. After administration of r-Antidote, the total plasma concentrations of the inhibitors increased to 1.9±0.09 μM, 2.0±0.4 μM and 4.2±0.7 μM, respectively, and the percentage of unbound inhibitor declined to 0%, 0.3%±0.1% and 0.05%±0.02%, respectively. Thus, for each of the three inhibitors, correction of prothrombin time by r-Antidote to near-normal values is associated with a reduction in the free fraction of the inhibitor[2].				
Solvent&Solubility		In Vitro: DMSO : 22 mg/mL (48.68 mM; Need ultrasonic and warming)				
		Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg	10 mg
			1 mM	2.2128 mL	11.0641 mL	22.1283 mL
			5 mM	0.4426 mL	2.2128 mL	4.4257 mL
		10 mM	0.2213 mL	1.1064 mL	2.2128 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℃，6 months; -20℃，1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。						
References		[1]. Zhang P, et al. Discovery of Betrixaban (PRT054021), N-(5-chloropyridin-2-yl)-2-(4-(N,N-dimethylcarbamimidoyl)benzamido)-5-methoxybenzamide, a highly potent, selective, and orally efficacious factor Xa inhibitor. Bioorg Med Chem Lett. 2009 Apr 15;19(8):21 [2]. Lu G, et al. A specific antidote for reversal of anticoagulation by direct and indirect inhibitors of coagulation factor Xa. Nat Med. 2013 Apr;19(4):446-51.				
实验参考:						
		Rats[2] Whole-blood INR values (mean±s.d.) in rats infused with Betrixaban (1 mg/kg per hour) or vehicle				



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Animal Administration	and then treated with either vehicle or r-Antidote by i.v. bolus (6 mg) over 5 min plus infusion (9 mg/h) for up to 90 min. Circles, vehicle+vehicle; squares, Betrixaban + vehicle; triangles, Betrixaban + r-Antidote. * $P \leq 0.02$ compared to the r-Antidote treatment group determined by unpaired two-tailed t test. Whole-blood INR values (mean \pm s.d.) in rats infused with Apixaban (0.5 mg per kg body weight h ⁻¹) or vehicle and then treated with either vehicle or r-Antidote by i.v. bolus (6 mg) over 5 min plus infusion (6 mg/h) for up to 90 min. Circles, vehicle + vehicle; squares, apixaban + vehicle; triangles, apixaban+r-Antidote. * $P \leq 0.01$ compared to the r-Antidote treatment group determined by unpaired two-tailed t test.
Kinase Assay	To measure the inhibition of fXa activity by direct fXa inhibitors and the reversal of its inhibitory effect by r-Antidote, purified human plasma fXa (3 nM) (Haematologic Technologies), varying concentrations of inhibitor (0, 2.5, 5.0 and 7.5 nM) and r-Antidote are added to the assay buffer (20 mM Tris, 150 mM NaCl, 5 mM Ca ²⁺ and 0.1% BSA, pH 7.4). After incubation at room temperature for 30 min, 100 μ M Spectrozyme-fXa is added to the mixture, and the initial rate of sub-strate cleavage is monitored continuously for 5 min at 405 nm in a 96-well plate reader. The initial velocity of product formation as a function of inhibitor and r-Antidote concentrations is analyzed by Dynafit to estimate the binding affinity of r-Antidote to each inhibitor[2].
References	[1]. Zhang P, et al. Discovery of Betrixaban (PRT054021), N-(5-chloropyridin-2-yl)-2-(4-(N,N-dimethylcarbamimidoyl)benzamido)-5-methoxybenzamide, a highly potent, selective, and orally efficacious factor Xa inhibitor. Bioorg Med Chem Lett. 2009 Apr 15;19(8):21 [2]. Lu G, et al. A specific antidote for reversal of anticoagulation by direct and indirect inhibitors of coagulation factor Xa. Nat Med. 2013 Apr;19(4):446-51.

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