上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：INDEGLITAZAR
产品别名：PPM 204

生物活性：

Description	Indeglitazar is an orally available peroxisome proliferator-activated receptor (PPAR) pan-agonist for all three PPAR subtypes alpha (α), delta (δ) and gamma (γ).		
IC_{50} & Target	PPARα	PPARδ	PPARγ
In Vitro	In an assay of preadipocyte differentiation, measuring in part functional insulin sensitization capability of the cells, Indeglitazar shows an EC50 of 0.32 μM compared with Rosiglitazone, which shows an EC50 of 13 nM, although the maximal response obtained from the 2 compounds is comparable[1].		
In Vivo	An initial assessment of in vivo activity is carried out using the Zucker rat model of diabetes. The significant lowering of glucose, HbA_{1C}, triglycerides, and total cholesterol are observed after i.v. treatment with 10 mg/kg Indeglitazar once per day for 3 weeks. Notably, the level of Adiponectin (on day 21) is essentially unchanged in treated vs. untreated animals (4.8 mcg/mL vs. 4.9 mcg/mL), thus the observed reductions in glucose and HbA_{1C} are achieved in an adiponectin-independent fashion. These differences in the effects of Indeglitazar in vivo may be a consequence of synergy between the 3 PPAR activities or because of the SPPARM profile of the compound, or a combination of these factors. The oral activity of Indeglitazar is assessed in the *ob/ob* model of diabetes and insulin resistance. Indeglitazar significantly decreases glucose, insulin, triglycerides, and free fatty acid levels[1].		
Solvent&Solubility	***In Vitro:*** **DMSO : 33 mg/mL (84.74 mM;** Need ultrasonic)		

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5679 mL	12.8396 mL	25.6792 mL
	5 mM	0.5136 mL	2.5679 mL	5.1358 mL
	10 mM	0.2568 mL	1.2840 mL	2.5679 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。

References	[1]. Artis DR, et al. Scaffold-based discovery of Indeglitazar, a PPAR pan-active anti-diabetic agent. Proc Natl Acad Sci U S A. 2009 Jan 6;106(1):262-7.

实验参考：

Animal Administration	Rats[1] Indeglitazar is administered once daily i.v. as a solution (10% SolutolHS15,10%ethanol,80%saline) to ZDF/GmiCrl-fa/fa rats. Treatment is initiated at age 7-8 weeks, and blood samples are analyzed before the treatment and 21 days after the treatment. Mice[1] Ob/ob mouse study. Indeglitazar (10 mg/kg) or Pioglitazone (30 mg/kg) are orally administered to 9-week-old B6.V-Lepob mice for 14 days. Compounds are suspected in 0.5% methylcellulose and

	2% Tween 80 before dosing. On the last day, blood is collected for insulin, triglyceride, free fatty acid, and adiponectin measurements.
Kinase Assay	The purified PPAR_ LBD protein is diluted to 12 mg/mL and 1mM of Indeglitazar and 2x molar excess of steroid receptor coactivator-1 (SRC-1) peptide are added before crystallization by mixing equal volumes of a protein/compound sample with reservoir solution containing 27% polyethylene glycol (PEG) 4000, 0.1 M 2-(bis-(2-hydroxy-ethyl)-amino)-2-hydroxymethyl- propane-1,3-diol (BisTris) buffer at pH 6.5, 0.2 M ammonium acetate, and 5% glycerol. The crystals are soaked in cryo-protective buffer (30% PEG 4000, 0.1 M BisTris buffer at pH 6.5, 0.2 M ammonium acetate, and 5% glycerol) before flash-freezing in liquid nitrogen for data collection[1].
References	[1]. Artis DR, et al. Scaffold-based discovery of Indeglitazar, a PPAR pan-active anti-diabetic agent. Proc Natl Acad Sci U S A. 2009 Jan 6;106(1):262-7.