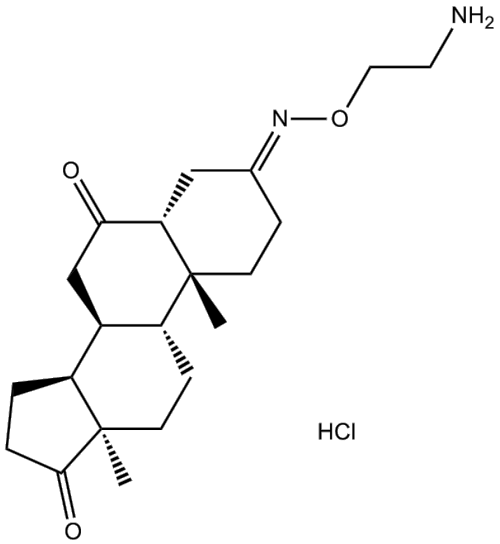
Product Data Sheet

Product Name: Istaroxime hydrochloride
Cat. No.: GC17786

Chemical Properties

Cas. No.	374559-48-5		
Chemical Name	(5S,8R,9S,10R,13S,14S)-3-(2-aminoethoxyimino)-10,13-dimethyl-1,2,4,5,7,8,9,11,12,14,15,16-dodecahydrocyclopenta[a]phenanthrene-6,17-dione;hydrochloride		
SMILES	CC12CCC(=NOCCN)CC1C(=O)CC3C2CCC4(C3CCC4=O)C.Cl		
Formula	$C_{21}H_{33}ClN_2O_3$	M.Wt	396.95
Solubility	DMSO : ≥ 45 mg/mL (113.36 mM); H_2O : 25 mg/mL (62.98 mM; Need ultrasonic)	Storage	4°C, sealed storage, away from moisture
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment: [1]

Product Data Sheet

Cell lines	Guinea pig ventricular myocytes
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.
Reaction Conditions	4 μM, 0.5 s
Applications	Resting Ca2+ was similarly increased by istaroxime (from 61.3 to 92.4 nM). Istaroxime increased [Ca]SR-tot by 47%. Istaroxime increased the amount of Ca2+ extruded by the Na+/Ca2+ exchanger (CaNCX) during caffeine-induced transients (+130). Istaroxime shortened the time elapsing between the start of the caffeine pulse and SR Ca2+ release.

Animal experiment: [2]

Animal models	Bio TO.2 hamsters and Bio F1B hamsters
Dosage form	Oral administration, 30 mg/5 mL/kg/day

Product Data Sheet

Applications	Heart function of istaroxime-treated hamsters was comparable to that of healthy animals, and had a significantly higher LVSP and both positive and negative dP/dT when compared with that of vehicle-treated animals. Coronary flow rate in hearts isolated from istaroxime-treated hamsters was higher than that from vehicle-treated Bio TO.2 animals. Besides that, Bio TO.2 hamsters treated with istaroxime had both time and frequency domain indexes of HRV, i.e. standard deviation of R-R intervals, TP, LF and HF, augmented with respect to vehicle-treated animals. Moreover , the LF/HF ratio of istaroxime-treated animals was similar to that observed in Bio F1B hamsters.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1] Rocchetti M, Besana A, Mostacciuolo G, et al. Modulation of sarcoplasmic reticulum function by Na+/K+ pump inhibitors with different toxicity: digoxin and PST2744 [(E, Z)-3-((2-aminoethoxy) imino) androstane-6, 17-dione hydrochloride]. Journal of Pharmacology and Experimental Therapeutics, 2005, 313(1): 207-215.

[2] Giudice P L, Mattera G G, Gagnol J P, et al. Chronic istaroxime improves cardiac function and heart rate variability in cardiomyopathic hamsters. Cardiovascular drugs and therapy, 2011, 25(2): 133-138.

Background

Istaroxime hydrochloride(PST2744) is a novel inhibitor of Na+/K+-ATPase with IC50 value of 0.43±0.15μM [1].

In vitro studies show that Istaroxime can inhibit the activity of Na+/K+-ATPase from dog kidney without significant interaction with other several receptors. It demonstrates the selectivity of Istaroxime. Ex vivo studies show the inotropic effect can be achieved up to 60% for Istaroxime.

Product Data Sheet

Istaroxime can also increase the force of contraction of guinea pig paced left atria in the range 0.3 to 30μM. In vivo assays prove Istaroxime is consistently safer than digoxin [1].

Istaroxime is a steroidal drug unrelated to cardiac glycosides that improves cellular calcium cycling. The inhibition of Na+/K+-ATPase induces cytosolic calcium accumulation during systole (inotropism). Clinical studies has been done with istaroxime in phase II. Istaroxime could be a promising alternative for patients with acute heart failure syndrome for whom the therapeutic options are currently limited [2].

References:

[1] R. Micheletti, G. G. Mattera, M. Rocchetti, A. Schiavone, M. F. Loi, A. Zaza, R. J. P. Gagnol, S. De Munari, P. Melloni, P. Carminati, G. Bianchi, and P. Ferrari. Pharmacological profile of the novel inotropic agent (e,z)-3-((2-aminoethoxy)imino)androstane-6,17-dione hydrochloride (PST2744). The journal of pharmacology and experimental therapeutics. 2002, 303 (2): 592-600.
[2] Suruchi Aditya, Aditya Rattan. Istaroxime: A rising star in acute heart failure. Journal of Pharmacology and Pharmacotherapeutics. 2012, 3(4): 353-355.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA