

Data Sheet

Product Name: Anamorelin (hydrochloride)

 Cat. No.:
 CS-1037

 CAS No.:
 861998-00-7

 Molecular Formula:
 C31H43CIN6O3

Molecular Weight: 583.16
Target: GHSR

Pathway: GPCR/G Protein

Solubility: DMSO : \geq 28 mg/mL (48.01 mM)

BIOLOGICAL ACTIVITY:

Anamorelin hydrochloride is a novel **ghrelin receptor** agonist with **EC**₅₀ value of 0.74 nM in the FLIPR assay. IC50 & Target: Ki: 0.7 nM (ghrelin receptor)^[1]

EC50: 0.74 nM (ghrelin receptor)^[1] **In Vitro:** In the FLIPR assay, Anamorelin (ANAM) shows significant agonist activity on the ghrelin receptor, with EC₅₀ value of 0.74 nM. No significant antagonist activity is observed with Anamorelin at concentrations of up to 1,000 nM. In the binding experiments, Anamorelin binds to the ghrelin receptor with a binding affinity constant (K_i) of 0.70 nM. In the competition assay with radiolabeled ibutamoren (35 S-MK-677; another ghrelin receptor agonist) Anamorelin (ANAM) is also found to bind with high affinity to the ghrelin receptor (IC_{50} =0.69 nM). In rat pituitary cells incubated with Anamorelin, there is a dose-dependent stimulatory effect on GH release and the potency (IC_{50}) is 1.5 nM. Anamorelin is screened for activity against a set of over 100 receptors, ion channels, transporters, and enzymes. Anamorelin demonstrates binding to the tachykinin neurokinin 2 (IC_{50} =0.021 IIM); however, a subsequent IIM, functional assay demonstrates no functional activity^[1]. In Vivo: In rats, Anamorelin (ANAM) at an oral dose of 3, 10, or 30 mg/kg once daily significantly increases both food intake and body weight from Day 2 to Day 7 of treatment compared with the vehicle control. The cumulative change in food intake and weight gain increases dose-dependently, and these changes are significant at all dose levels (IIM-0.05) compared to the control. Administration of Anamorelin at a single oral dose of 3, 10, or 30 mg/kg induces a dose-dependent increase in plasma GH levels and GH AUC_{0-6h} in rats^[1].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: ^[1]For the competition assay, Anamorelin (ANAM) concentrations (1 pM-10 μM) are added to the membranes together with ³⁵S-MK-677. Nonspecific binding is determined by adding 10 μM nonlabeled MK-677. The mixture is incubated at 30°C for 60 min, followed by application of the samples to GF/B filters, which has been pretreated with 0.5 % PEI for 60 min. The filters are subsequently washed in 0.9 % NaCl and counted using an OptiPhase counter^[1]. **Animal Administration**: Anamorelin (ANAM) is stored frozen at -20°C under protection from light until use, when it is dissolved and serially diluted in distilled water to concentrations of 6, 2, and 0.6 mg/mL for administration. These working solutions are stored protected from light at 5°C and used within 6 days^[1]. [^{1]}Rats^[1] For the assessment of food intake and body weight, rats are divided into four groups: Anamorelin 3 mg/kg (n=7), 10 mg/kg (n=7), or 30 mg/kg (n=7), or vehicle control (n=8), and 100 μL blood samples are collected before and 0.25, 0.5, 1, 2, 3, 4, 5, and 6 h after single dosing. Rats are anesthetized with sodium pentobarbital 64.8 mg/kg. A catheter filled with heparinized saline solution is inserted in the left femoral artery for blood collection and fitted with an extension tube, 1 mL sampling syringe, and a three-way cock to allow excess blood to return. Plasma levels of GH are measured immunochemically using a Rat Growth Hormone EIA kit and microplate reader. Measurements are performed in duplicate. Area under the GH concentration curve from 0 to 6 h (AUC_{0-6h}) postdose and the time course of GH plasma concentrations are evaluated.

Pig^[1]

In pigs (n=6 per group), Anamorelin is dosed directly into the gastric lumen via the dosing catheter. Blood samples are collected for

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the stimulation profile of GH at 30 and 15 min before, and 0, 5, 15, 30, 45, 60, and 120 min following dosing. Animals received either a single dose (3.5 mg/kg), or once-daily administration (1 mg/kg) for 7 days and stimulation profiles are taken after the first and seventh dose of Anamorelin. To assess IGF-1 levels, pigs receive either placebo or Anamorelin for 7 days (1 mg/kg/day), and the following 7 days the two treatments are crossed over. A single blood sample is taken once a day immediately before dosing.

References:

[1]. Pietra C, et al. Anamorelin HCl (ONO-7643), a novel ghrelin receptor agonist, for the treatment of cancer anorexia-cachexiasyndrome: preclinical profile. J Cachexia Sarcopenia Muscle. 2014 Dec;5(4):329-37.

CAIndexNames:

3-Piperidinecarboxylic acid, 1-[(2R)-2-[(2-amino-2-methyl-1-oxopropyl)amino]-3-(1H-indol-3-yl)-1-oxopropyl]-3-(phenylmethyl)-, 1,2,2-trimethylhydrazide, hydrochloride (1:1), (3R)-

SMILES:

Caution: Product has not been fully validated for medical applications. For research use only.

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