Print Date: Nov 12th 2019

Certificate of Analysis

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Product Name: **PHA 665752** **Catalog No.: 2693** **Batch No.: 3**

CAS Number: 477575-56-7

IUPAC Name: (2*R*)-1-[[5-[(*Z*)-[5-[[(2,6-Dichlorophenyl)methyl]sulfonyl]-1,2-dihydro-2-oxo-3*H*-indol-3-ylidene]methyl]-2,4-dimethyl-1*H*-pyrrol-3-yl]carbonyl]-2-(1-pyrrolidinylmethyl)pyrrolidine

1. PHYSICAL AND CHEMICAL PROPERTIES

Batch Molecular Formula: $C_{32}H_{34}Cl_2N_4O_4S.½H_2O$

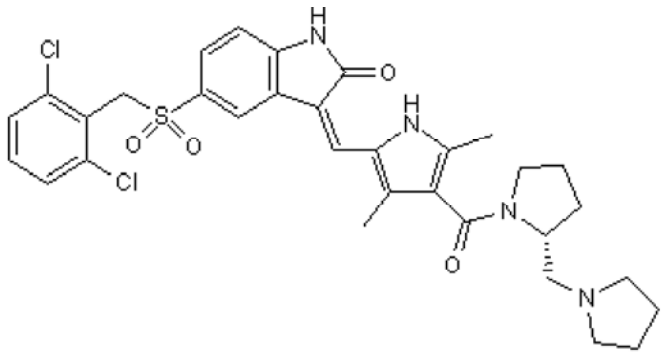
Batch Molecular Weight: 650.62

Physical Appearance: Yellow solid

Solubility: DMSO to 100 mM

Storage: Store at +4°C

Batch Molecular Structure:



2. ANALYTICAL DATA

TLC: R_f = 0.2 (Dichloromethane:Methanol [9:1])

HPLC: Shows 98.5% purity

Chiral HPLC: Shows 98.6% purity

^{1}H NMR: Consistent with structure

Mass Spectrum: Consistent with structure

Optical Rotation: $[\alpha]_D$ = +47 (Concentration = 1, Solvent = Methanol)

Microanalysis:

	Carbon	Hydrogen	Nitrogen
Theoretical	59.07	5.42	8.61
Found	58.98	5.3	8.53

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Description:

Potent, selective and ATP-competitive inhibitor of MET kinase (IC_{50} values are 9, 68, 200, 1400, 3000, 3800 and 6000 nM for MET, Ron, Flk-1, c-abl, FGFR1, EGFR and c-src respectively and > 10000 nM for IGF-IR, PDGFR, AURORA2, PKA, PKBα, p38α, MK2 and MK3). Antitumor agent; inhibits tumorigenicity and angiogenesis in mouse lung cancer xenografts.

Physical and Chemical Properties:

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Minimum Purity: >98%

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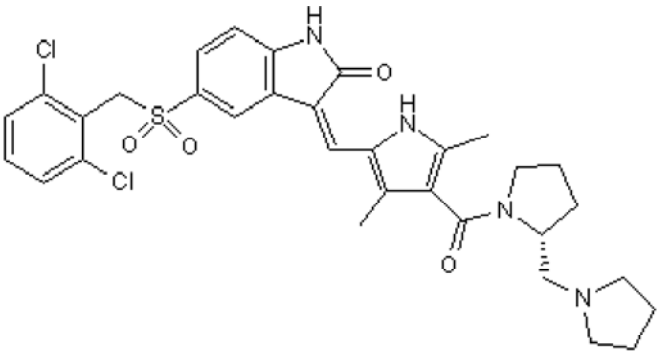

Storage: Store at +4°C

Solubility & Usage Info:

DMSO to 100 mM

Stability and Solubility Advice:

Some solutions can be difficult to obtain and can be encouraged by rapid stirring, sonication or gentle warming (in a 45-60°C water bath).

Information concerning product stability, particularly in solution, has rarely been reported and in most cases we can only offer a general guide. Our standard recommendations are:

SOLIDS: Provided storage is as stated on the product label and the vial is kept tightly sealed, the product can be stored for up to 6 months from date of receipt.

SOLUTIONS: We recommend that stock solutions, once prepared, are stored aliquoted in tightly sealed vials at -20°C or below and used within 1 month. Wherever possible solutions should be made up and used on the same day.

Other Information:

INFORMATION FOR CUSTOMERS IN THE UK ONLY

This product is a Schedule 1 Home Office controlled substance and customers in the UK are required to hold the relevent licence or be exempt from restrictions in order to purchase and posess this material.

Licensing Information:

Sold for research purposes under agreement from Pfizer Inc.

References:

Tu *et al* (2010) Efficacy of c-Met inhibitor for advanced prostate cancer. BMC Cancer ***10*** 556. PMID: 20946682.

Puri *et al* (2007) A selective small molecule inhibitor of c-Met, PHA665752, inhibits tumorigenicity and angiogenesis in mouse lung cancer xenografts. Cancer Res. ***67*** 3529. PMID: 17440059.

Smolen *et al* (2006) Amplification of MET may identify a subset of cancers with extreme sensitivity to the selective tyrosine kinase inhibitor PHA-665752. Proc.Natl.Acad.Sci.USA ***103*** 2316.

Christensen *et al* (2003) A selective small molecule inhibitor of c-Met kinase inhibits c-Met-dependent phenotypes in vitro and exhibits cytoreductive antitumour activity *in vivo*. Cancer Res. ***63*** 7345. PMID: 14612533.