

PRODUCT INFORMATION

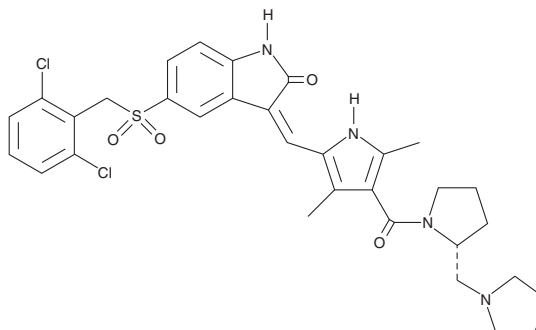


PHA-665752

Item No. 14703

CAS Registry No.: 477575-56-7

Formal Name: (3Z)-5-[[[2,6-dichlorophenyl)methyl]sulfonyl]-3-[[3,5-dimethyl-4-[[[(2R)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]-1H-pyrrol-2-yl]methylene]-1,3-dihydro-2H-indol-2-one



MF: $C_{32}H_{34}Cl_2N_4O_4S$

FW: 641.6

Purity: $\geq 98\%$

UV/Vis.: λ_{max} : 309, 439 nm

Supplied as: A crystalline solid

Storage: $-20^{\circ}C$

Stability: ≥ 4 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

PHA-665752 is supplied as a crystalline solid. A stock solution may be made by dissolving the PHA-665752 in the solvent of choice. PHA-665752 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of PHA-665752 in these solvents is approximately 1, 10, and 25 mg/ml, respectively.

PHA-665752 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PHA-665752 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. PHA-665752 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The c-Met receptor tyrosine kinase and its ligand, hepatocyte growth factor, have been implicated in the development and progression of several human cancers.¹ PHA-665752 is an ATP-competitive, active-site inhibitor of the catalytic activity of c-Met kinase ($K_i = 4$ nM; $IC_{50} = 9$ nM).² It exhibits >50-fold selectivity for c-Met over a panel of tyrosine and serine/threonine kinases. PHA-665752 can inhibit c-Met phosphorylation, as well as cell proliferation and cell motility, of various tumor cells ($IC_{50}s = 18-50$ nM).² It also inhibits signal transduction downstream of c-Met, interfering with the activation of Gab-1 adaptor protein, ERK1/2, Akt, STAT3, PLC- γ , and focal adhesion kinase in multiple tumor cell lines.² In a gastric carcinoma xenograft model, 25 mg/kg PHA-665752 was shown to reduce tumor growth in mice by inhibiting c-Met activation.²

References

1. Mughal, A., Aslam, H.M., Sheikh, A., *et al.* c-Met inhibitors. *Infect. Agent. Cancer* 8, 13 (2013).
2. Christensen, J.G., Schreck, R., Burrows, J., *et al.* A selective small molecule inhibitor of c-Met kinase inhibits c-Met-dependent phenotypes *in vitro* and exhibits cytoreductive antitumor activity *in vivo*. *Cancer Res.* 63(21), 7345-7355 (2003).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY

Buyer agrees to purchase the material subject to Cayman's Terms and Conditions. Complete Terms and Conditions including Warranty and Limitation of Liability information can be found on our website.

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