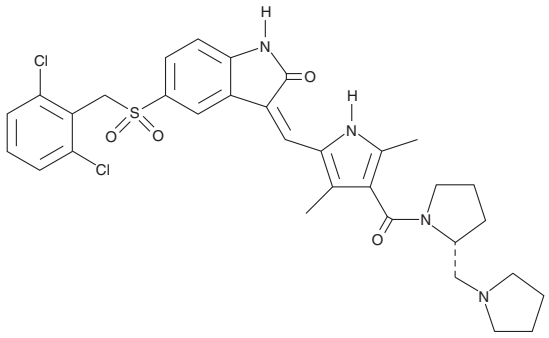
# PRODUCT INFORMATION

## 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:** ≥98%
**UV/Vis.:** $\lambda_{max}$: 309, 439 nm
**Supplied as:** A crystalline solid
**Storage:** -20°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).





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