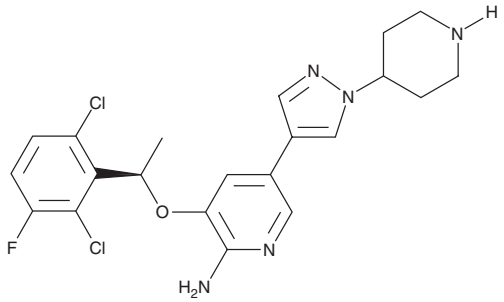
PRODUCT INFORMATION

(R)-Crizotinib

Item No. 12087

CAS Registry No.:	877399-52-5
Formal Name:	3-[(1R)-1-(2,6-dichloro-3-fluorophenyl) ethoxy]-5-[1-(4-piperidinyl)-1H-pyrazol-4-yl]-2-pyridinamine
Synonym:	PF 2341066
MF:	$C_{21}H_{22}Cl_2FN_5O$
FW:	450.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 206, 269, 323 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

(R)-Crizotinib is supplied as a crystalline solid. A stock solution may be made by dissolving the (R)-crizotinib in the solvent of choice, which should be purged with an inert gas. (R)-Crizotinib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of (R)-crizotinib in ethanol and DMSO is approximately 0.5 mg/ml and approximately 5 mg/ml in DMF.

(R)-Crizotinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, (R)-crizotinib should first be dissolved in DMF and then diluted with the aqueous buffer of choice. (R)-Crizotinib 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

(R)-Crizotinib is a dual inhibitor of c-Met and anaplastic lymphoma kinase (ALK; IC_{50}s = 8 and 20 nM, respectively, in a cell-based assay).[1] It is selective for c-Met and ALK over several other receptor- and non-receptor tyrosine kinases, including Ron, Tie2, Abl, LCK, and VEGFR2 (IC_{50}s = 0.08, 0.448, 1.159, 2.741, and >10 µM, respectively). (R)-Crizotinib selectively inhibits the proliferation of cancer cell lines with *MET* amplifications over cancer cell lines with *MET* or *EGFR* mutations (IC_{50}s = 5-10, 472-1,284, and 767-787 nM, respectively).[2] It induces apoptosis in *MET*-amplified EBC-1 and NCI H1993 lung cancer cells when used at a concentration of 100 nM. (R)-Crizotinib (25 mg/kg) reduces tumor volume in an EBC-1 mouse xenograft model. Formulations containing crizotinib have been used in the treatment of metastatic, relapsed, or refractory ALK-positive cancers.

References

1. Cui, J.J., Tran-Dubé, M., Shen, H., *et al*. Structure based drug design of crizotinib (PF-02341066), a potent and selective dual inhibitor of mesenchymal-epithelial transition factor (c-MET) kinase and anaplastic lymphoma kinase (ALK). *J. Med. Chem.* **54(18)**, 6342-6363 (2011).
2. Tanizaki, J., Okamoto, I., Okamoto, K., *et al*. MET tyrosine kinase inhibitor crizotinib (PF-02341066) shows differential antitumor effects in non-small cell lung cancer according to MET alterations. *J. Thorac. Oncol.* **6(10)**, 1624-1631 (2011).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM