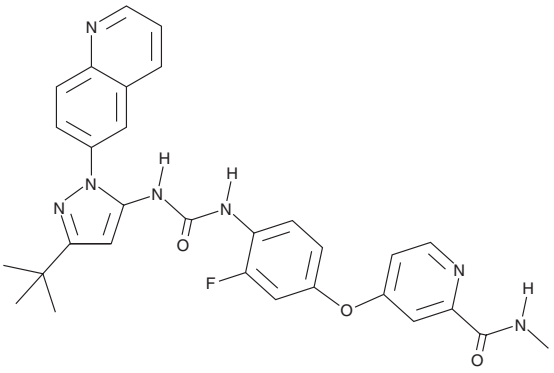
PRODUCT INFORMATION

Rebastinib

Item No. 21465



CAS Registry No.:	1020172-07-9
Formal Name:	4-[4-[[[[3-(1,1-dimethylethyl)-1-(6-quinolinyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-3-fluorophenoxy]-N-methyl-2-pyridinecarboxamide
Synonym:	DCC-2036
MF:	$C_{30}H_{28}FN_7O_3$
FW:	553.6
Purity:	≥98%
UV/Vis.:	λ_{max}: 251 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

Rebastinib is supplied as a crystalline solid. A stock solution may be made by dissolving the rebastinib in the solvent of choice, which should be purged with an inert gas. Rebastinib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of rebastinib in ethanol is approximately 1 mg/ml and approximately 30 mg/ml in DMSO and DMF.

Rebastinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, rebastinib should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Rebastinib has a solubility of approximately 0.33 mg/ml in a 1:2 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Rebastinib is an orally bioavailable tyrosine kinase inhibitor that inhibits Abl1 (IC_{50} = 0.8 nM) as well as the gatekeeper mutant $Abl1^{T315I}$ (IC_{50} = 4 nM) and the activation loop mutant $Abl1^{H396P}$.[1] It also inhibits the Src family kinases Src, Lyn, Fgr, and Hck and the tyrosine kinases KDR, FLT3, and Tie2 at nanomolar concentrations. Rebastinib inhibits mutant $Abl1^{T315I}$ signaling and prolongs survival in a mouse Ba/F3 cell allograft model.[1,2] Rebastinib also exhibits *in vivo* antineoplastic activity against cells with the T674I point mutation of FIP1-like-1-platelet-derived growth factor receptor α.[3]

References

1. Chan, W.W., Wise, S.C., Kaufman, M.D., *et al.* Conformational control inhibition of the BCR-ABL1 tyrosine kinase, including the gatekeeper T315I mutant, by the switch-control inhibitor rebastinib. *Cancer Cell.* **19(4)**, 556-568 (2011).
2. Eide, C.A., Adrian, L.T., Tyner, J.W., *et al.* The ABL switch control inhibitor rebastinib is active against the chronic myeloid leukemia mutant $BCR\text{-}ABL^{T315I}$ and exhibits a narrow resistance profile. *Cancer Res.* **71(9)**, 3189-3195 (2011).
3. Shen, Y., Shi, X., and Pan, J. The conformational control inhibitor of tyrosine kinases rebastinib is effective for imatinib-resistant cells expressing T674I FIP1L1-PDGFRα. *PLoS One* **8(8)**, e73059 (2013).

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