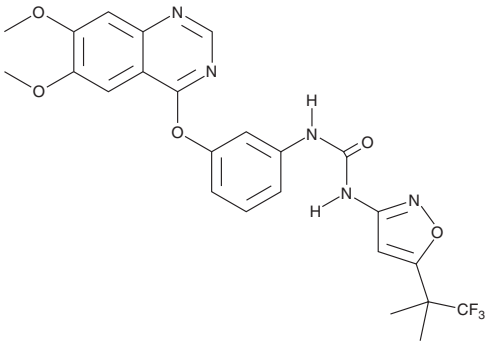
PRODUCT INFORMATION

CEP-32496

Item No. 18776

CAS Registry No.:	1188910-76-0
Formal Name:	N-[3-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[5-(2,2,2-trifluoro-1,1-dimethylethyl)-3-isoxazolyl]-urea
MF:	$C_{24}H_{22}F_3N_5O_5$
FW:	517.5
Purity:	≥95%
UV/Vis.:	λ_{max}: 239, 319 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

CEP-32496 is supplied as a crystalline solid. A stock solution may be made by dissolving the CEP-32496 in the solvent of choice, which should be purged with an inert gas. CEP-32496 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of CEP-32496 in these solvents is approximately 2, 20, and 10 mg/ml, respectively.

CEP-32496 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, CEP-32496 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. CEP-32496 has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

B-Raf is a MAP kinase kinase kinase, which functions downstream of Ras family GTPases to activate MEK1/2 and ERK1/2 signaling.[1] Mutations of B-Raf, particularly at Val^{600}, are common in melanomas and melanocytic nevi.[1] CEP-32496 is a potent inhibitor of B-Raf^{V600E} (K_d = 14 nM in an *in vitro* binding assay).[2] It blocks B-Raf^{V600E}-dependent phosphorylation of MEK in human melanoma A375 and colorectal cancer COLO 205 cells (IC_{50}s = 78 and 60 nM, respectively).[2] CEP-32496 binds kinases other than B-Raf but displays selective cytotoxicity for cells expressing B-Raf^{V600E}.[2] It displays good oral bioavailability in rats, dogs, and monkeys and has single oral dose pharmacodynamics inhibition of both pMEK and pERK in B-Raf^{V600E} colon carcinoma xenografts in nude mice.[2]

References

1. Tronnier, M. and Mitteldorf, C. Treating advanced melanoma: Current insights and opportunities. *Cancer Manag. Res.* **6**, 349-356 (2014).
2. James, J., Ruggeri, B., Armstrong, R.C., *et al.* CEP-32496: A novel orally active $BRAF^{V600E}$ inhibitor with selective cellular and *in vivo* antitumor activity. *Mol. Cancer Ther.* **11(4)**, 930-941 (2012).

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