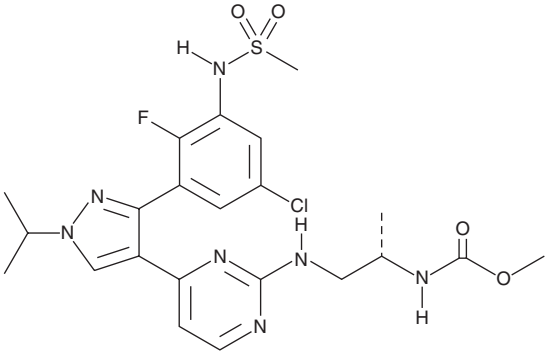
PRODUCT INFORMATION

Encorafenib

Item No. 16994

CAS Registry No.:	1269440-17-6
Formal Name:	N-[(1S)-2-[[4-[3-[5-chloro-2-fluoro-3-[(methylsulfonyl)amino]phenyl]-1-(1-methylethyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]amino]-1-carbamic acid, methyl ester
Synonym:	LGX818
MF:	$C_{22}H_{27}ClFN_7O_4S$
FW:	540.0
Purity:	≥98%
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

Encorafenib is supplied as a crystalline solid. A stock solution may be made by dissolving the encorafenib in the solvent of choice, which should be purged with an inert gas. Encorafenib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of encorafenib in these solvents is approximately 15, 20, and 25 mg/ml, respectively.

Encorafenib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, encorafenib should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Encorafenib 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

B-Raf is a MAP kinase kinase kinase, which functions downstream of Ras family GTPases to activate MEK1/2 and ERK1/2 signaling. A mutation of B-Raf in exon 15 at codon 600 where a valine is substituted by glutamic acid (V600E) has been linked to melanoma.[1] Encorafenib is a selective inhibitor of B-Raf^{V600E} mutant melanoma cell proliferation (EC_{50} = 4 nM) with little activity against wild-type B-Raf or a panel of 100 other kinases (IC_{50}s = 900 nM).[1] At oral doses of 6 mg/kg in human melanoma xenograft models, encorafenib was shown to decrease phosphorylation of the B-Raf substrate MEK.[3]

References

1. Tronnier, M. and Mitteldorf, C. Treating advanced melanoma: Current insights and opportunities. *Cancer Manag. Res.* **6**, 349-356 (2014).
2. Stuart, D.D., Li, N., Poon, D.J., *et al.* Preclinical profile of LGX818: A potent and selective RAF kinase inhibitor. *Cancer Res.* **72**, (2012).
3. Huang, T., Karsy, M., Zhuge, J., *et al.* B-Raf and the inhibitors: From bench to bedside. *J. Hematol. Oncol.* **6**, 1-9 (2013).

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