

PRODUCT INFORMATION



Dabrafenib

Item No. 16989

CAS Registry No.: 1195765-45-7

Formal Name: N-[3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-4-thiazolyl]-2-fluorophenyl]-2,6-difluoro-benzenesulfonamide

Synonym: GSK2118436

MF: C₂₃H₂₀F₃N₅O₂S₂

FW: 519.6

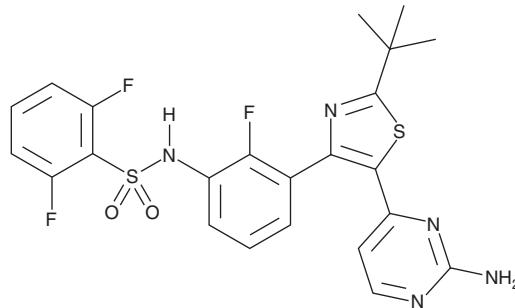
Purity: ≥98%

UV/Vis.: λ_{max}: 281, 333 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

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

Dabrafenib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, dabrafenib should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Dabrafenib has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Dabrafenib is an ATP-competitive inhibitor of Raf kinases (IC₅₀s = 0.64, 0.68, and 5 nM for wild-type B-RAF kinase, mutant B-RAF^{V600E}, and wild-type C-RAF kinase, respectively).¹ It also inhibits the tyrosine kinase-like kinases ALK5 and LIMK1 (IC₅₀s = 11 and 15 nM, respectively) and the calcium/calmodulin-dependent protein kinases SIK2 and PDK2 (IC₅₀s = 27 and 57 nM, respectively), as well as NEK11, CK1, and BRK (IC₅₀s = 20, 41, and 79 nM, respectively) in a panel of 270 kinases at 300 nM. Dabrafenib inhibits the growth of 16 cancer cell lines expressing mutant B-RAF^{V600E} (GI₅₀s = <200 nM), five cell lines expressing other B-RAF mutants (GI₅₀s = <30 nM), and 19 cell lines expressing wild-type Ras and RAF (GI₅₀s = <7,000 nM). However, it does not inhibit the growth of four cancer cell lines expressing mutant B-RAF^{V600E}, 133 cell lines expressing wild-type Ras and Raf, or 18 cell lines expressing mutant Ras (GI₅₀s = >10 μM) in a panel of 195 cancer cell lines. Dabrafenib (8 nM) inhibits MAPK signaling, inhibiting phosphorylation of MEK and ERK, and activates caspase-3/7 in B-RAF^{V600E}-expressing A375P melanoma cells but not in wild-type B-RAF-expressing human foreskin fibroblasts (EC₂₀₀s = 71 and >10,000 nM, respectively). It reduces tumor growth in an A375P mouse xenograft model when administered at doses ranging from 3 to 100 mg/kg. Formulations containing dabrafenib have been used in the treatment of B-RAF^{V600E}-expressing cancers.

Reference

- King, A.J., Arnone, M.R., Bleam, M.R., et al. Dabrafenib; Preclinical characterization, increased efficacy when combined with trametinib, while BRAF/MEK tool combination reduced skin lesions. *PLoS One* **8**(7), e67583 (2013).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY

Buyer agrees to purchase the material subject to Cayman's Terms and Conditions. Complete Terms and Conditions including Warranty and Limitation of Liability information can be found on our website.

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