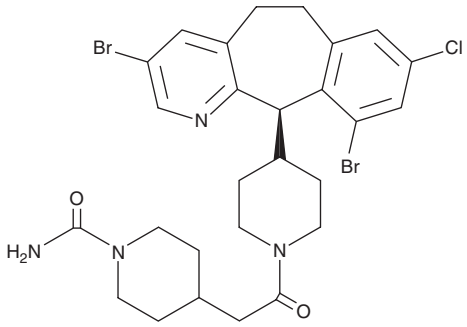
PRODUCT INFORMATION

Lonafarnib

Item No. 11746

CAS Registry No.: 193275-84-2
Formal Name: 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-1-piperidinecarboxamide
Synonyms: Sarasar, SCH 66336
MF: $C_{27}H_{31}Br_2ClN_4O_2$
FW: 638.8
Purity: ≥98%
UV/Vis.: λ_{max}: 278 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

Lonafarnib is supplied as a crystalline solid. A stock solution may be made by dissolving the lonafarnib in the solvent of choice, which should be purged with an inert gas. Lonafarnib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of lonafarnib in ethanol and DMF is approximately 14 mg/ml and approximately 3 mg/ml in DMSO.

Lonafarnib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, lonafarnib should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. Lonafarnib has a solubility of approximately 0.2 mg/ml in a 1:4 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Farnesyltransferase drives the post-translational farnesylation of a number of target proteins, including Ras, a component of the MAPK and Akt signaling pathways involved in cell proliferation, and Ras homolog enriched in brain (Rheb), which stimulates mTOR activity.[1] By arresting growth, farnesyltransferase inhibitors have great potential as antitumor agents. Lonafarnib is a farnesyltransferase inhibitor that blocks the post-translational lipid modification of oncogenic Ras isoforms H-Ras, N-Ras, and K-Ras (IC_{50}s = 1.9, 2.8, and 5.2 nM, respectively) as well as Rheb (IC_{50} = 10-100 nM).[2,3] It inhibits H-Ras signaling in whole cells (IC_{50} = 10 nM) and blocks the transformed growth properties of fibroblasts (IC_{50} = 75 nM) and human tumor cell lines (IC_{50} = 400 nM) expressing activated K-Ras proteins. In the nude mouse, lonafarnib demonstrates potent dose-dependent oral activity in an array of human tumor xenograft models including tumors originating from colon, lung, pancreas, prostate, and urinary bladder.[2] Combination treatments with various cytotoxic agents (cyclophosphamide, 5-fluorouracil, and vincristine) or MAPK or Akt pathway inhibitors can enhance the *in vivo* efficacy of lonafarib.[2,4]

References

1. Appels, N.M.G.M., Beijnen, J.H., and Schellens, J.H.M. *Oncologist* **10(8)**, 565-578 (2005).
2. Liu, M., Bryant, M.S., Chen, J., *et al. Cancer Res.* **58(21)**, 4947-4956 (1998).
3. Basso, A.D., Mirza, A., Liu, G., *et al. J. Biol. Chem.* **280(35)**, 31101-31108 (2005).
4. Niessner, H., Beck, D., Sinnberg, T., *et al. J. Invest. Dermatol.* **131(2)**, 468-479 (2011).

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